Reeves
08/817507

-key terms

(FILE 'CAPLUS' ENTERED AT 14:13:04 ON 15 JAN 1999)
DEL HIS Y
L1 1599 SEA ABB=ON PLU=ON PLASMACYTOS? OR PLASMACYTOMA OR PLASMA(W)(CYTOSIS OR CYTOM?) OR CASTELMAN?(W)(DISEAS? OR DISORDER)
L2 114 SEA ABB=ON PLU=ON L1(S)(TREAT? OR THERAP?)
L3 14 SEA ABB=ON PLU=ON L2 AND (MOAB OR MAB OR MONOCLON? OR (PMI OR PM1 OR PM(W)(1 OR I))(W)ANTIBOD? OR BP2998 OR BP 2998)

=> d 1-14 .beverly

L3 ANSWER 1 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:469373 CAPLUS
DN 129:243873
TI Induction of apoptosis in plasmacytoma cells by a cytotoxic factor secreted by P388D1 macrophage-like cell line
SO Int. J. Immunother. (1998), 14(2), 69-81
CODEN: IJIMET; ISSN: 0255-9625
AU Chu, C. -Y.; Liu, T. -H.; Tseng, J.
PY 1998
AB Tumoricidal activity is one of the major effector functions of activated macrophages. A previous study demonstrated that the culture supernatant of P388D1 murine macrophage-like cells showed a cytotoxic effect on plasmacytoma MOPC-315, MPC-11, and myeloma FO but had no effect on J558 myeloma cells. Here, the plasmacytoma cytotoxic factor in P388D1 culture supernatant was partially purified by a DEAE-Sephacel ionic-exchanger chromatog. and a panel of **monoclonal** antibodies against plasmacytoma cytotoxic factor was prepd. All **monoclonal** antibodies partially blocked the P388D1-mediated tumoricidal activity. A large-scale purifn. was performed by ammonium sulfate fractionation (40-60% satn.), followed by immunoaffinity chromatog. using one of the anti-plasmacytoma cytotoxic factor **monoclonal** antibodies, CB7-C2. The affinity-purified plasmacytoma cytotoxic factor had IC50 at 3.11 .mu.g/mL for 2.times.104 MOPC-315 cells and showed a major band with an estd. mol. wt. of 62 kDa on SDS-PAGE gels. However, CB7.C2 recognized a single band with an estd. mol. wt. of 120-130 kDa on Western blotting, suggesting that the native form of the plasmacytoma cytotoxic factor could be a dimer. Plasmacytoma cytotoxic factor-mediated cytotoxicity involved apoptosis. Data from both agarose gel electrophoresis and terminal deoxynucleotidyl transferase-mediated deoxyuridine 5-triphosphate (dUTP) nick-end-labeling method indicated that a significant amt. of DNA fragmentation was induced in **plasmacytoma** cytotoxic factor-**treated** MOPC-315 cells. Using an Annexin V staining technique, the **plasmacytoma** cytotoxic factor-induced apoptosis was confirmed further by observing the phosphatidylserine redistribution on the plasma membrane of

plasmacytoma cytotoxic factor-**treated** cells. The plasmacytoma cytotoxic factor-induced apoptosis was dose-dependent and time-dependent and could be neutralized by CB7.C2 anti-plasmacytoma cytotoxic factor antibody. Thus, a 62 kDa protein secreted by P388D1 macrophage-like cells shows its cytotoxic effect on MOPC-315 plasmacytoma cells via induction of apoptosis.

L3 ANSWER 2 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:439936 CAPLUS
DN 129:183744
TI Therapy of plasma cell malignancies
SO Basic Clin. Oncol. (1998), 14(Medical Management of Hematological Malignant Diseases), 281-307
CODEN: BCLOEQ; ISSN: 1073-0028
AU Giles, Francis J.
PY 1998
AB A review with 66 refs. This article reviews the pathophysiol., diagnosis, staging, and treatment with and without stem cell transplantation for multiple myeloma. **Treatment** of solitary **plasmacytoma** of bone, extramedullary **plasmacytoma**, **monoclonal** gammopathy of uncertain significance, and future prospects for anti-multiple myeloma **therapy** are discussed.

L3 ANSWER 3 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1998:308281 CAPLUS
DN 129:64963
TI Irradiated IL-2 gene-modified plasmacytoma vaccines are more efficient than live vaccines
SO Int. J. Oncol. (1998), 12(5), 1195-1198
CODEN: IJONES; ISSN: 1019-6439
AU Simova, Jana; Bubenik, Jan; Jandlova, Tana; Indrova, Marie
PY 1998
AB The effect of irradn. on the **therapeutic** efficacy of IL-2 gene-modified **plasmacytoma** cells used as a vaccine in the immunotherapy of parental murine **plasmacytoma** X63-Ag8.653 was examd. Local administration of the IL-2-secreting plasmacytoma irradiated with a dose of 50 Gy inhibited i.p. plasmacytoma growth more effectively than the administration of non-irradiated, live cell vaccines. Whereas the vaccination with the live cell vaccine could substantially prolong the survival of the tumor-bearing mice but did not significantly induce tumor regressions, the irradiated vaccines could substantially increase the no. of tumor-free animals. The irradiated vaccines produce higher amts. of IL-2 than the live cell vaccines both in vitro and in vivo. Depletion of CD4+ and CD8+ effector cells with **monoclonal** antibodies has significantly decreased the effect of the vaccination. It can be concluded that both, CD4+ and CD8+ T lymphocytes are required for effective IL-2 gene **therapy** of the X63-Ag8.653

plasmacytoma and that the higher effect of the irradiated vaccines is probably due to their higher IL-2 prodn.

L3 ANSWER 4 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1997:75834 CAPLUS
DN 126:203608
TI Cytomedical **therapy** for IgG1 **plasmacytosis** in human interleukin-6 transgenic mice using hybridoma cells microencapsulated in alginate-poly(L-lysine)-alginate membrane
SO Biochim. Biophys. Acta (1997), 1360(1), 53-63
CODEN: BBACAQ; ISSN: 0006-3002
AU Okada, Naoki; Miyamoto, Hajime; Yoshioka, Tatsunobu; Katsume, Asao; Saito, Hiroyuki; Yorozu, Keigo; Ueda, Otoya; Itoh, Norio; Mizuguchi, Hiroyuki; Nakagawa, Shinsaku; Ohsugi, Yoshiyuki; Mayumi, Tadanori
PY 1997
AB Cytomedical therapy for human interleukin-6 transgenic mice (hIL-6 Tgm) was implemented by the i.p. injection of alginate-poly(L)lysine-alginate (APA) membranes microencapsulating SK2 hybridoma cells (APA-SK2 cells) which secrete anti-hIL-6 **monoclonal** antibodies (SK2 **mAb**). IgG1 plasmacytosis in the hIL-6 Tgm was suppressed by a single injection of APA-SK2 cells, and the survival time of these mice was remarkably prolonged. The viable cell no. and the SK2 **mAb**-secretion of APA-SK2 cells increased for at least one month both under culture conditions and in allogeneic recipients (in vivo). Moreover, SK2 **mAb** which were secreted from APA-SK2 cells injected into allogeneic recipients was detected in serum at high concns.; 3-5 mg/mL from day 14 to day 50 post-injection. In contrast, the injection of free SK2 cells had no therapeutic effect on hIL-6 Tgm. These results strongly suggest that APA membranes microencapsulating cells which were modified to secrete mols. useful for the treatment of a disorder were effective as an in vivo long-term delivery system of bioactive mols., as 'cytomedicine'.

L3 ANSWER 5 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1996:693193 CAPLUS
DN 126:135486
TI Medical application of microencapsulating hybridoma cells in agarose microbeads 'cytomedicine': **therapeutic** effect on IgG1 **plasmacytosis** and mesangio-proliferative glomerulonephritis in the interleukin 6 transgenic mouse
SO J. Controlled Release (1997), 44(2,3), 195-200
CODEN: JCREEC; ISSN: 0168-3659
AU Okada, Naoki; Miyamoto, Hajime; Kaneda, Yoshihisa; Yamamoto, Yoko; Katsume, Asao; Saito, Hiroyuki; Yorozu, Keigo; Ueda, Otoya; Tsutsumi, Yasuo; et al.
PY 1997
AB We conducted preliminary studies to examine the feasibility of using microencapsulated living cells as carriers of bioactive drugs

('cytomedicine') to test our premise that such a novel drug delivery system would have certain advantages as a long-term delivery system for hormones, enzymes and other biomols. in vivo. As graft rejection occurs when living cells are implanted in allogeneic or xenogeneic recipients, accordingly we used agarose microencapsulation technique to prevent destruction of the implanted cells by the host's immune system. Human interleukin 6 (hIL-6) transgenic mice, which develop massive IgG1 plasmacytosis and mesangio-proliferative glomerulonephritis with age, were i.p. injected with agarose microbeads contg. SK2 hybridoma cells (SK2 cells), which secrete anti-hIL-6 **monoclonal** antibodies. These mice demonstrated **therapeutic** response with reduced IgG1 **plasmacytosis** and proteinuria, and they also showed prolongation of survival time compared with the untreated group. These results are encouraging evidence that cytomedicine has potential application as an effective long-term delivery system of bioactive drugs in vivo.

L3 ANSWER 6 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1996:386117 CAPLUS
DN 125:56234
TI Remedy for diseases caused by IL-6 production
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

	APPLICATION NO.	DATE
AI	WO 95-JP2169	19951020
	AU 95-37099	19951020
	JP 95-272893	19951020
	EP 95-934866	19951020
	HU 97-1900	19951020
	FI 97-1669	19970418
	NO 97-1816	19970418

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9612503	A1	19960502	WO 95-JP2169	19951020
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, KE, KG, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9537099	A1	19960515	AU 95-37099	19951020
	AU 689657	B2	19980402		
	JP 08169846	A2	19960702	JP 95-272893	19951020
	EP 791359	A1	19970827	EP 95-934866	19951020
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

	HU 77035	A2	19980302	HU 97-1900	19951020
	FI 9701669	A	19970617	FI 97-1669	19970418
	NO 9701816	A	19970618	NO 97-1816	19970418

PY 1996
1996
1998
1996
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1997

AB A preventive or remedy for diseases caused by interleukin-6 prodn., contg. an antibody against interleukin-6 receptors (an IL-6R antibody). Examples of the antibody include antibodies of animals other than humans, such as mouse and rat, chimeric antibodies comprising the above antibodies and a human antibody, and a reconstituted human antibody. Examples of the diseases concerned include plasmacytosis, anti-IgG1-emia, anemia and nephritis.

L3 ANSWER 7 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1994:628470 CAPLUS
DN 121:228470
TI Low-dose melphalan-induced shift in the production of a Th2-type cytokine to a Th1-type cytokine in mice bearing a large MOPC-315 tumor
SO Cancer Immunol. Immunother. (1994), 39(2), 117-26
CODEN: CIIMDN; ISSN: 0340-7004
AU Gorelik, Leonid; Prokhorova, Anna; Mokyr, Margalit B.
PY 1994
AB The current studies demonstrate that MOPC-315 tumor cells secrete large amts. of interleukin-10 (IL-10), which contributes to the inhibitory activity of MOPC-315 culture supernatants for the in vitro generation of antitumor cytotoxicity by MOPC-315-"immune" spleen cells. Moreover, addn. of neutralizing **monoclonal** anti-IL-10 antibody to the in vitro stimulation cultures of cells from the tumor infiltrated spleens of mice bearing a large MOPC-315 tumor resulted in the generation of enhanced anti-MOPC-315 cytotoxicity. In contrast, addn. of **monoclonal** anti-IL-10 antibody to the in vitro stimulation cultures of splenic cells from mice that are in the final stages of immune-mediated tumor eradication as a consequence of low-dose melphalan (L-phenylalanine mustard; L-PAM) therapy (and whose spleens no longer contain metastatic tumor cells) did not lead to enhancement in the in vitro generation of antitumor cytotoxicity. The cessation of IL-10 secretion as a consequence of low-dose L-PAM therapy of MOPC-315 tumor bearers was found to be accompanied by the acquisition of the ability to secrete interferon .gamma. (IFN.gamma.) by the splenic cells. In addn., by day 2 after low-dose L-PAM therapy a drastic decrease in the amt. of IL-10 secreted by the s.c. tumor nodules was

noted, which preceded the accumulation of tumor-infiltrating lymphocytes capable of secreting IFN.gamma.. Thus, low-dose L-PAM therapy of mice bearing a large MOPC-315 tumor leads to a shift in cytokine prodn. from a Th2-type cytokine to a Th1-type cytokine, and it is conceivable that this shift in cytokine prodn. plays an important role in the low-dose L-PAM-induced acquisition of antitumor immunity by hitherto immunosuppressed mice bearing a large MOPC-315 tumor.

L3 ANSWER 8 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1994:315321 CAPLUS
DN 120:315321
TI Gene therapy of cancer: use of IL-2 gene transfer and kinetics of local T and NK cell subsets
SO Anticancer Res. (1993), 13(5A), 1457-60
CODEN: ANTRD4; ISSN: 0250-7005
AU Bubenik, Jan; Zeuthen, Jesper; Bubenikova, Dana; Simova, Jana; Jandlova, Tana
PY 1993
AB Expts. were designed to compare the efficacy of recombinant IL-2 immunotherapy and IL-2 gene **therapy** of i.p. growing murine **plasmacytoma** X63-Ag8.653. The kinetics of peritoneal exudate mononuclear cells were monitored during the progression and gene **therapy** of the **plasmacytoma**, using cytofluorometric anal. and **monoclonal** antibodies against T and NK cell subsets. It has been found that the percentage of mice protected against **plasmacytoma** transplants was higher in mice **treated** by transfer of genetically manipulated IL-2-producing **plasmacytoma** cells as compared to the mice repeatedly injected with recombinant IL-2. I.p. inoculation of the X63-Ag8.653 plasmacytoma led in most of the inoculated mice to an increased percentage of NK+, ASGM1+, Thy 1.2+, CD3+ and TCR.alpha..beta.+ cells in the peritoneal fluid. The presence of macroscopically detectable i.p. tumors was accompanied by a higher increase in the percentage of NK+ and TCR.gamma..delta.+ cells. Local IL-2 gene **therapy** of the **plasmacytoma** either prevented or diminished an increase in the percentage of CD3+, Thy 1.2+ and TCR.alpha..beta.+ lymphocytes.

L3 ANSWER 9 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1994:161352 CAPLUS
DN 120:161352
TI Oncostatin M, leukemia inhibitory factor, and interleukin 6 induce the proliferation of human plasmacytoma cells via the common signal transducer, gp130
SO J. Exp. Med. (1994), 179(4), 1343-7
CODEN: JEMEAV; ISSN: 0022-1007
AU Nishimoto, Norihiro; Ogata, Atsushi; Shima, Yoshihito; Tani, Yoshihiko; Ogawa, Hiroyasu; Nakagawa, Masashi; Sugiyama, Haruo;

Yoshizaki, Kazuyuki; Kishimoto, Tadamitsu

PY 1994

AB The authors analyzed the stimulatory effect of oncostatin M (OSM), leukemia inhibitory factor (LIF), interleukin 6 (IL-6), IL-11, and the inhibitory effect of anti-IL-6 antibody (Ab), anti-IL-6 receptor **monoclonal** antibody (**mAb**), and anti-gp130 **mAb** on the growth of human plasmacytoma cells freshly isolated from a patient with multiple myeloma. The purified cells showed a plasmacytoid morphol. and expressed CD38, CD54, and CD56 antigens but no CD3, CD5, CD10, CD19, CD20, or very late antigen 5. IL-6 receptor (IL-6R) and its signal transducer, gp130, were expressed on their cell surface at a low level. Dose-dependent proliferation of the cells in response to OSM, LIF, and IL-6, but not to IL-11, was obsd. using [3H]TdR incorporation in vitro. Both anti-IL-6 Ab and anti-IL-6R **mAb** inhibited the growth of the cells in the presence or absence of exogenous IL-6. These cells release IL-6 but not OSM or LIF into the culture supernatant during short-term culture. Therefore, an autocrine growth mechanism mediated by IL-6, but not by OSM or LIF, was confirmed. Furthermore, anti-gp130 **mAb** completely inhibited the proliferation of the cells induced by OSM, LIF, as well as IL-6. These data indicate that OSM, LIF, and IL-6 can act as growth factors of human **plasmacytoma** cells through a common signal transducer, gp130, on their cell surface, and also suggest the potential **therapeutic** application of anti-gp130 **mAb**, as well as anti-IL-6R **mAb** against myeloma/ **plasmacytomas**.

L3 ANSWER 10 OF 14 CAPLUS COPYRIGHT 1999 ACS

AN 1994:243 CAPLUS

DN 120:243

TI Involvement of TCR-V.beta.8.3+ cells in the cure of mice bearing a large MOPC-315 tumor by low dose melphalan

SO J. Immunol. (1993), 151(9), 4838-46
CODEN: JOIMA3; ISSN: 0022-1767

AU Mokyr, Margalit B.; Rubin, Michael; Newell, Kenneth A.; Prokhorova, Anna; Bluestone, Jeffrey A.

PY 1993

AB The authors have previously shown that the curative efficacy of low dose melphalan (L-phenylalanine mustard; L-PAM) for mice bearing a large s.c. MOPC-315 tumor requires the participation of CD8+ (but not CD4+) T cell-dependent antitumor immunity. Here the authors show that CD8+ T cells obtained from regressing tumors on day 4 or 5 after low dose L-PAM therapy of MOPC-315 tumor bearers (L-PAM TuB mice) display a preferential enhancement in the utilization of the TCR-V.beta.8.3 gene segment as compared to CD8+ T cells form normal lymph nodes. Treatment of L-PAM TuB mice with **monoclonal** antibody (**mAb**) F23.1, which leads to the depletion of V.beta.8.3+ cells, as well as V.beta.8.1 and 8.2+ cells, led to a

significant redn. in the ability of their tumor-infiltrating lymphocytes as well as their spleen cells to lyse MOPC-315 tumor cells in vitro in a short term assay. In addn., the **mAb** F23.1 **treatment** almost completely abrogated the lytic activity of the tumor-infiltrating lymphocytes against another syngeneic, antigenically related **plasmacytoma** (the MOPC-104E). Moreover, the **mAb** F23.1 treatment significantly reduced the curative effectiveness of low dose L-PAM for mice bearing a large MOPC-315 tumor. In contrast, **mAb** KJ16 treatment, which leads to the depletion of V.beta.8.1 and 8.2+ cells (but not V.beta.8.3+ cells), did not reduce significantly the curative effectiveness of low dose L-PAM for such MOPC-315 tumor bearers. Thus, V.beta.8.3+ T cells are important for the curative effectiveness of low dose L-PAM **therapy** for MOPC-315 tumor bearers, and it is conceivable that the V.beta.8.3+ cells mediate their effect (at least in part) by contributing to the acquisition of CTL activity against **plasmacytoma**-shared Ag.

L3 ANSWER 11 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1991:469832 CAPLUS
DN 115:69832
TI **Monoclonal** antibodies to interleukin-6 and their medical use
SO Ger., 8 pp.
CODEN: GWXXAW
IN Wijdenes, John; Clement, Claude; Morel-Fourrier, Brigitte; Peters, Andre; Kloft, Michael; Sebald, Walter; Schwulera, Udo

	APPLICATION NO.	DATE
AI	DE 89-3939706	19891201
	EP 90-122694	19901128
	JP 90-337033	19901130
	BR 90-6128	19901203

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3939706	C1	19910321	DE 89-3939706	19891201
	EP 430193	A1	19910605	EP 90-122694	19901128
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 03232485	A2	19911016	JP 90-337033	19901130
	BR 9006128	A	19910924	BR 90-6128	19901203

PY 1991
1991
1991
1991

AB **Monoclonal** antibodies BE-4, BE-8, and BF-6 to interleukin-6 (IL-6) are produced by the std. hybridoma method for use in therapy, prophylaxis, and diagnosis (e.g. by sandwich ELISA) of IL-6-mediated diseases. BE-4 and BE-8 compete with IL-6 for IL-6 receptors on human and mouse cell lines and inhibit the

proliferation of IL-6-dependent cell lines; BF-6 lacks these activities, but recognizes receptor-bound IL-6. All 3 antibodies bind to different epitopes on IL-6. Patients with end-stage multiple myeloma **treated** with BE-4 showed marked clin. improvement and decrease in **plasmacytoma** cell no.

L3 ANSWER 12 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1991:17244 CAPLUS
DN 114:17244
TI Importance of tumor-specific cytotoxic CD8+ T-cells in eradication of a large subcutaneous MOPC-315 tumor following low-dose melphalan therapy
SO Cancer Res. (1990), 50(23), 7641-9
CODEN: CNREA8; ISSN: 0008-5472
AU Takesue, Blaine Y.; Pyle, Joseph M.; Mokyr, Margalit B.
PY 1990
AB It was previously demonstrated that depletion of CD8+ T-cells by the use of a **monoclonal** anti-Lyt-2.2 antibody abolishes the curative effectiveness of low-dose melphalan (L-phenylalanine mustard; L-PAM) therapy for BALB/c mice bearing a large (.gtoreq.20 mm) s.c. MOPC-315 tumor and extensive metastases. Here it is shown that as a consequence of low-dose L-PAM therapy, CD8+ T-cells accumulate in the s.c. tumor nodules of MOPC-315 tumor bearers. Specifically, an 80-fold increase in the no. of CD8+ T-cells was seen within 5 days after the chemotherapy. Treatment of MOPC-315 tumor bearers with low-dose L-PAM in conjunction with **monoclonal** anti-Thy-1.2 or anti-Lyt-2.2 antibody, in contrast to treatment with **monoclonal** anti-L3T4 antibody, prevented the appearance of the massive CD8+ T-cell infiltrate in the s.c. tumor nodules. Fresh CD8+ T-cells derived from s.c. MOPC-315 tumor nodules that were regressing as a consequence of low-dose L-PAM **therapy** exhibited a potent direct lytic activity against the MOPC-315 **plasmacytoma** in a short-term in vitro assay. The specificity of the lytic activity exhibited by the CD8+ T-cells to lyse two antigenically unrelated thymomas (the WEHI 22.1 and the EL-4) and a natural killer-sensitive lymphoma (the YAC-1), but also by their relatively weak lytic activity against an antigenically related plasmacytoma (the MOPC-104E). Thus, CD8+ T-cells that infiltrate the s.c. tumor nodules of MOPC-315 tumor bearers following low-dose L-PAM therapy most likely exploit a CTL-type lytic mechanism to eradicate at least part of the large tumor burden not eliminated by the direct antitumor effects of the drug.

L3 ANSWER 13 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1990:530455 CAPLUS
DN 113:130455
TI Mouse plasmacytoma growth in vivo: enhancement by interleukin 6 (IL-6) and inhibition by antibodies directed against IL-6 or its

receptor
SO J. Exp. Med. (1990), 172(3), 997-1000
CODEN: JEMEAV; ISSN: 0022-1007
AU Vink, Anne; Coulie, Pierre; Warnier, Guy; Renauld, Jean Christophe; Stevens, Monique; Donckers, Dominique; Van Snick, Jacques
PY 1990
AB Murine plasmacytomas show a striking dependence on interleukin 6 (IL-6) for their growth in vitro. Here, evidence is presented suggesting that IL-6 also plays an essential role in the in vivo development of these tumors. This conclusion is based on the finding that the tumorigenicity of an IL-6-dependent **plasmacytoma** cell line was increased .apprx.100-fold on transfection with an IL-6 expression vector, whereas it was inhibited in animals **treated** with **monoclonal** antibodies capable of blocking the binding of IL-6 to its receptor. Injection of these antibodies 1 day before tumor challenge protected >50% of the mice and retarded tumor growth in all animals. Tumors arising in antibody-treated mice retained their IL-6 dependence in vitro, suggesting that the level of protection could be improved if stronger IL-6 antagonists were available.

L3 ANSWER 14 OF 14 CAPLUS COPYRIGHT 1999 ACS
AN 1984:628262 CAPLUS
DN 101:228262
TI Protection against infection with Pseudomonas aeruginosa by passive transfer of **monoclonal** antibodies to lipopolysaccharides and outer membrane proteins
SO J. Infect. Dis. (1984), 150(4), 570-6
CODEN: JIDIAQ; ISSN: 0022-1899
AU Sawada, Shuzo; Suzuki, Masahiko; Kawamura, Takashi; Fujinaga, Shigeki; Masuho, Yasuhiko; Tomibe, Katsuhiko
PY 1984
AB Exptl. infection with P. aeruginosa was **treated** with 8 different **monoclonal** antibodies (MCAs) produced by hybridoma cells obtained through cell fusion of mouse **plasmacytoma** cells and spleen cells from mice immunized with a virulent strain of P. aeruginosa (Homma serotype 7). Five MCAs bound to lipopolysaccharides (LPSs) specific to serotype 7 or serotypes 2, 7, and 13, whereas the other 3 MCAs bound with broad specificities to outer membrane protein (OMP) fractions. The MCAs to LPS were highly protective against infection, with 50% protective doses of 0.05-2.5 .mu.g Ig/mouse. In contrast, the MCAs to OMP were much less protective, with a 50% protective dose range of 10->100 .mu.g IgG/mouse. Most of the MCAs to LPS agglutinated P. aeruginosa cells, but all the MCAs to OMP produced so far have not, although all the MCAs bound well to the cells. Agglutinating MCAs provided better protection than did nonagglutinating MCAs.

=> d his 14-

(FILE 'USPATFULL' ENTERED AT 14:18:50 ON 15 JAN 1999)
L4 37 S L3
L5 28 S L4 AND ADMIN?

=> d 1-28 .bevpat

L5 ANSWER 1 OF 28 USPATFULL
AN 1999:1474 USPATFULL
TI Reshaped human antibody to human interleukin-6
IN Tsuchiya, Masayuki, Gotenba, Japan
Sato, Koh, Gotenba, Japan
Hirata, Yuichi, Gotenba, Japan
PA Chugai Seiyaku Kabushiki Kaisha, Tokyo, Japan (non-U.S. corporation)
PI US 5856135 990105
WO 9428159 941208
AI US 96-553501 960220 (8)
WO 94-JP859 940530
960220 PCT 371 date
960220 PCT 102(e) date
PRAI JP 93-129787 930531
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Vavarro, Mark
LREP Foley & Lardner
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1672
AB A reshaped antibody comprising:

(A) L chains comprising:

(1) a human C region, and

(2) an L chain V region comprising human L chain FRs and L chain CDRs of a mouse **monoclonal** antibody; and

(B) H chains comprising:

(1) a human H chain C region, and

(2) an H chain V region comprising human H chain FRs, and H chain cDRs of a mouse **monoclonal** antibody to human IL-6. Since the major portions of the reshaped human antibody are derived from human, and the mouse CDRs are less immunogenic, then the present reshaped human antibody is less immunogenic, and therefore

inhibits information transfer by IL-6, and is promising as a therapeutic agent for diseases caused by IL-6.

INCL INCLM: 435/069.300
INCLS: 435/069.600; 435/070.210; 435/320.100; 435/326.000; 435/328.000; 435/332.000; 435/335.000; 536/023.530

L5 ANSWER 2 OF 28 USPATFULL
AN 1998:147218 USPATFULL
TI Methods for diagnosis of conditions associated with elevated levels of telomerase activity
IN West, Michael D., Belmont, CA, United States
Shay, Jerry, Dallas, TX, United States
Wright, Woodring, Arlington, TX, United States
PA University of Texas System Board of Regents, Austin, TX, United States (U.S. corporation)
PI US 5840495 981124
AI US 95-480037 950607 (8)
RLI Division of Ser. No. US 93-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489508 which is a continuation-in-part of Ser. No. US 92-882438, filed on 13 May 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Myers, Carla J.
LREP Kaster, KevinLyon & Lyon LLP
CLMN Number of Claims: 27
ECL Exemplary Claim: 7
DRWN 16 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2663
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to inhibit telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.100
INCLS: 435/004.000; 435/006.000; 435/015.000; 435/091.200; 435/091.500; 436/064.000; 436/501.000; 935/077.000; 935/078.000

L5 ANSWER 3 OF 28 USPATFULL
AN 1998:134800 USPATFULL
TI Method for screening for agents which increase telomerase activity in a cell
IN West, Michael D., San Carlos, CA, United States

Shay, Jerry, Dallas, TX, United States
Wright, Woodring E., Arlington, TX, United States
PA Geron Corporation, Menlo Park, CA, United States (U.S. corporation)
Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5830644 981103
AI US 93-151477 931112 (8)
RLI Continuation-in-part of Ser. No. US 93-60952, filed on 13 May 1993 which is a continuation-in-part of Ser. No. US 93-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489508 which is a continuation-in-part of Ser. No. US 92-882438, filed on 13 May 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Myers, Carla J.
LREP Kaster, Kevin; Warburg, Richard J.; Hellenkamp, Amy S.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 54 Drawing Figure(s); 42 Drawing Page(s)
LN.CNT 5675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to increase or decrease telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity and means are shown for slowing or reversing the loss of telomeric repeats in aging cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/004.000; 435/091.200; 435/007.200; 435/015.000; 436/034.000; 436/063.000; 436/064.000; 436/094.000; 436/501.000; 935/077.000; 935/078.000

L5 ANSWER 4 OF 28 USPATFULL
AN 1998:131550 USPATFULL
TI Method of detecting myocardial infarction
IN Matsumori, Akira, Minoo, Japan
PA Akira Matsumori, Osaka-Fu, Japan (non-U.S. corporation)
Otsuka Pharmaceutical Co., Ltd., Tokyo-To, Japan (non-U.S. corporation)
PI US 5827673 981027
AI US 96-696160 960813 (8)
DT Utility
EXNAM Primary Examiner: Housel, James C.; Assistant Examiner: Ryan, V.

LREP Sughrue, Mion, Zinn, Macpeak & Seas, PLLC
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 598
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of detecting and diagnosing myocardial infarction which detects myocardial infarction by immunoassay using a **monoclonal** antibody having specific reactivity for human hepatocyte growth factor (HGF) as obtained by using human HGF as immunogen as well as a disganostic agent for myocardial infarction which comprises, as essential component thereof, the **monoclonal** antibody mentioned above. The method of the present invention makes it possible to detect and diagnose patients with myocardial infarction.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.920
INCLS: 435/007.940; 436/536.000; 436/540.000; 436/548.000; 436/811.000; 436/815.000; 530/380.000; 530/403.000

L5 ANSWER 5 OF 28 USPATFULL
AN 1998:127903 USPATFULL
TI Modulation of endothelial cell proliferation with IP-10
IN Luster, Andrew, Wellesley, MA, United States
Leder, Philip, Chestnut Hill, MA, United States
PA President & Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)
PI US 5824299 981020
AI US 95-493638 950622 (8)
DT Utility
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Basham, Daryl A.
LREP Clark & Elbing LLP
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 19 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods for modulating endothelial cell proliferation. Also, disclosed are methods of detecting compounds which inhibit IP-10 and PF4 binding to a HSPG receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.100
INCLS: 514/002.000

L5 ANSWER 6 OF 28 USPATFULL

AN 1998:104717 USPATFULL
TI Compound and method for inhibiting angiogenesis
IN Davidson, Donald J., Gurnee, IL, United States
PA Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
PI US 5801146 980901
AI US 96-643219 960503 (8)
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Stole, Einar
LREP Steele, Gregory W.; Casuto, Dianne
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 1500
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mammalian kringle 5 is disclosed as a compound for treating angiogenic diseases. Methods and compositions for inhibiting angiogenic diseases are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/012.000
INCLS: 530/380.000; 530/324.000; 530/300.000

L5 ANSWER 7 OF 28 USPATFULL
AN 1998:85932 USPATFULL
TI THF-.gamma.2 analogs and pharmaceutical compositions comprising them
IN Burstein, Yigal, Rehovot, Israel
Trainin, Nathan, Rehovot, Israel
PA Yeda Research and Development Company Ltd at Weizmann Institute of Science, Rehovot, Israel (non-U.S. corporation)
PI US 5783557 980721
WO 9501182 950112
AI US 96-571985 960329 (8)
WO 94-US7304 940628
960329 PCT 371 date
960329 PCT 102(e) date
PRAI IL 93-106214 930701
DT Utility
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Harle, Jennifer
LREP Kohn & Associates
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 956
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to analogs of thymic humoral factor .gamma.2 (THF-.gamma.2) having at least 4 amino acid residues and

corresponding to the sequence of THF-.gamma.2 of the formula I:

Leu-Glu-Asp-Gly-Pro-Lys-Phe-Leu I

but differing therefrom by addition, deletion or substitution of one or more amino acid residues, or by cyclization, or by linkage of two or more sequences (I) or modified sequences (I) either directly or through a peptidic or non-peptidic chain.

The THF-.gamma.2 analogs of the invention and the functional derivatives and salts thereof are for use as immunomodulatory in pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/011.000
INCLS: 514/002.000; 514/013.000; 514/014.000; 514/015.000; 514/016.000; 514/017.000; 514/018.000; 514/021.000; 514/885.000; 530/301.000; 530/327.000; 530/328.000; 530/329.000; 530/330.000; 530/331.000; 530/326.000; 424/095.000

L5 ANSWER 8 OF 28 USPATFULL
AN 1998:69155 USPATFULL
TI Soluble form of GMP-140
IN McEver, Rodger P., Oklahoma City, OK, United States
PA The Board of Regents of The University of Oklahoma, Norman, OK, United States (U.S. corporation)
PI US 5767241 980616
AI US 94-272224 940708 (8)
RLI Continuation of Ser. No. US 89-320408, filed on 8 Mar 1989, now patented, Pat. No. US 5378464
DT Utility
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Teng, Sally P.
LREP Dunlap & Codding, P.C.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1369
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to a purified soluble form of human granule membrane protein 140 (GMP-140) which lacks an amino acid sequence comprising a transmembrane domain and which is effective in inhibiting leukocyte adherence mediated by granule membrane protein 140. Nucleic acid encoding the soluble form of GMP-140 is disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/350.000

INCLS: 435/069.100; 435/325.000; 435/252.300; 435/254.110; 530/395.000; 536/235.000

L5 ANSWER 9 OF 28 USPATFULL
AN 1998:4398 USPATFULL
TI Therapy and diagnosis of conditions related to telomere length and/or telomerase activity
IN West, Michael D., Belmont, CA, United States
Shay, Jerry, Dallas, TX, United States
Wright, Woodring, Arlington, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5707795 980113
AI US 95-487290 950607 (8)
RLI Division of Ser. No. US 93-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489508, issued on 6 Feb 1996 which is a continuation-in-part of Ser. No. US 92-882438, filed on 13 May 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Myers, Carla J.
LREP Kaster, Kevin; Warburg, Richard J.; Hellenkamp, Amy S.
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2688
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to inhibit telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/005.000
INCLS: 435/006.000; 435/091.200; 435/004.000; 536/024.330; 436/063.000; 436/064.000; 935/078.000; 935/008.000

L5 ANSWER 10 OF 28 USPATFULL
AN 97:115098 USPATFULL
TI Telomerase activity assays for diagnosing pathogenic infections
IN West, Michael D., Belmont, CA, United States
Shay, Jerry, Dallas, TX, United States
Wright, Woodring, Arlington, TX, United States
Blackburn, Elizabeth H., San Francisco, CA, United States
McEachern, Michael J., San Francisco, CA, United States
PA University of Texas System, Austin, TX, United States (U.S.

corporation)
The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 5695932 971209
AI US 93-60952 930513 (8)
RLI Continuation-in-part of Ser. No. US 93-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489508 which is a continuation-in-part of Ser. No. US 92-882438, filed on 13 May 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Campbell, Eggerton A.
LREP Lyon & Lyon
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 44 Drawing Figure(s); 32 Drawing Page(s)
LN.CNT 4620
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to inhibit telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity and means are shown for slowing the loss of telomeric repeats in aging cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/091.100

L5 ANSWER 11 OF 28 USPATFULL
AN 97:112439 USPATFULL
TI Uses of TGF-.beta. receptor fragment as a therapeutic agent
IN Segarini, Patricia R., 38 Devonshire Ave., #5, Mountain View, CA, United States 94043
Dasch, James R., 837 Seminole, Redwood City, CA, United States 94062
Olsen, David R., 276 Hedge Rd., Menlo Park, CA, United States 94025
Carrillo, Pedro A., 1966 California St., #7, San Francisco, CA, United States 94109
Mascarenhas, Desmond, 1074 Morningside Dr., Sunnyvale, CA, United States 94087
PI US 5693607 971202
AI US 94-361873 941222 (8)
RLI Continuation of Ser. No. US 93-37597, filed on 26 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-968375, filed on 29 Oct 1992, now abandoned

DT Utility
EXNAM Primary Examiner: Fitzgerald, David L.
LREP Morrison & Foerster
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1545
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of treating TGF-.beta. excess is disclosed. The treatment is parenteral, oral or topical **administration** of TGF-.beta. receptor fragment. Particularly effective is a soluble receptor fragment which resembles the extracellular portion of TGF-.beta. binding protein II.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/002.000
INCLS: 514/008.000; 435/069.100

L5 ANSWER 12 OF 28 USPATFULL
AN 97:104277 USPATFULL
TI Methods for screening for agents which modulate telomere length
IN West, Michael D., Belmont, CA, United States
Shay, Jerry, Dallas, TX, United States
Wright, Woodring, Arlington, TX, United States
PA University of Texas System Board of Regents, Austin, TX, United States (U.S. corporation)
PI US 5686245 971111
AI US 95-475778 950607 (8)
RLI Division of Ser. No. US 93-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489508 which is a continuation-in-part of Ser. No. US 92-882438, filed on 13 May 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Myers, Carla J.
LREP Warburg, Richard J.; Hellenkamp, Amy S.; Kaster, Kevin
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2643
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to inhibit telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/006.000
INCLS: 435/091.200; 435/004.000; 435/091.100; 435/015.000; 935/077.000; 935/078.000; 514/044.000; 436/064.000

L5 ANSWER 13 OF 28 USPATFULL
AN 97:59050 USPATFULL
TI Therapy and diagnosis of conditions related to telomere length and/or telomerase activity
IN West, Michael D., San Carlos, CA, United States
Harley, Calvin B., Palo Alto, CA, United States
Strahl, Catherine M., San Francisco, CA, United States
McEachern, Michael J., San Francisco, CA, United States
Shay, Jerry, Dallas, TX, United States
Wright, Woodring E., Arlington, TX, United States
Blackburn, Elizabeth H., San Francisco, CA, United States
Vaziri, Homayoun, Toronto, Canada
PA Board of Reagents, The University of Texas System, Dallas, TX, United States (U.S. corporation)
The Reagents of the University of California, Oakland, CA, United States (U.S. corporation)
Geron Corporation, Menlo Park, CA, United States (U.S. corporation)
PI US 5645986 970708
AI US 93-153051 931112 (8)
RLI Continuation-in-part of Ser. No. US 93-60952, filed on 13 May 1993 which is a continuation-in-part of Ser. No. US 93-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489508 which is a continuation-in-part of Ser. No. US 92-882438, filed on 13 May 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Myers, Carla
LREP Kaster, Kevin R.; Warburg, Richard J.; Hellenkamp, Amy S.
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 55 Drawing Figure(s); 43 Drawing Page(s)
LN.CNT 5798
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to increase or decrease telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity and means are shown for slowing or reversing the loss of telomeric repeats in aging cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/006.000
INCLS: 435/091.200; 435/183.000; 435/184.000; 435/194.000; 436/063.000; 536/024.310; 536/024.330

L5 ANSWER 14 OF 28 USPATFULL
AN 96:101447 USPATFULL
TI Anti-EDA **monoclonal** antibody and a method for diagnosis of disease associated with the EDA region of fibronectin
IN Sekiguchi, Kiyotoshi, Sakai, Japan
Asakawa, Kaneji, Tokushima, Japan
Sakashita, Eiji, Tokushima, Japan
Hino, Kazuo, Tokushima, Japan
Shin, Sadahito, Tokushima, Japan
Tachikawa, Tetsuya, Tokushima, Japan
Hirano, Hisanobu, Naruto, Japan
PA Otsuka Pharmaceutical Factory, Inc., Tokushima, Japan (non-U.S. corporation)
PI US 5571679 961105
AI US 93-119231 930922 (8)
PRAI JP 91-61524 910326
JP 91-157966 910628
JP 91-286668 911031
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.
LREP Sughrue, Mion, Zinn, Macpeak & Seas
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 921
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides an anti-EDA **monoclonal** antibody which recognizes an amino acid sequence portion in the EDA region of fibronectin (FN). The antibody of the invention has specific reactivity against EDA, in particular EDA-FN. By utilizing it, a simple and easy, high-sensitivity and high-precision immunoassay method for EDA-FN as well as a screening or diagnostic technique for EDA-FN-associated inflammatory and other diseases can be established.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/071.000
INCLS: 435/240.270; 530/388.250

L5 ANSWER 15 OF 28 USPATFULL
AN 96:82617 USPATFULL
TI Immunoassay for isothiazolones
IN Willingham, Gary L., Glenside, PA, United States
Schuman, Richard F., North Potomac, MD, United States
Huang, Chun-Hsien, Rockville, MD, United States

Chapman, John S., Ambler, PA, United States
PA Rohm and Haas Company, Philadelphia, PA, United States (U.S. corporation)
PI US 5554542 960910
AI US 93-128451 930928 (8)
RLI Continuation-in-part of Ser. No. US 92-927765, filed on 28 Sep 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Kepplinger, Esther M.; Assistant Examiner: Green, Lora M.
LREP Fein, Michael B.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 965
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immunoassay for isothiazolones based on **monoclonal** antibodies that react with isothiazolones, particularly, 5-chloro-2-methyl-3-isothiazolone, hybridomas that produce such antibodies, especially ATCC HB 11435, a method of preparing an immunogenic conjugate of isothiazolones and a macromolecule carrier, a method of producing **monoclonal** antibodies reactive with isothiazolones, and compositions comprising **monoclonal** or polyclonal antibodies reactive with isothiazolones.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/548.000
INCLS: 436/092.000; 436/815.000; 435/240.270; 530/388.900

L5 ANSWER 16 OF 28 USPATFULL
AN 96:11055 USPATFULL
TI Therapy and diagnosis of conditions related to telomere length and/or telomerase activity
IN West, Michael D., Belmont, CA, United States
Shay, Jerry, Dallas, TX, United States
Wright, Woodring, Arlington, TX, United States
PA University of Texas System Board of Regents, Austin, TX, United States (U.S. corporation)
PI US 5489508 960206
AI US 93-38766 930324 (8)
RLI Continuation-in-part of Ser. No. US 92-882438, filed on 13 May 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Myers, Carla
LREP Warburg, Richard; Kaster, Kevin; Stark, Amy
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 14 Drawing Page(s)

LN.CNT 2552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and compositions are provided for the determination of telomere length and telomerase activity, as well as the ability to inhibit telomerase activity in the treatment of proliferative diseases. Particularly, primers are elongated under conditions which minimize interference from other genomic sequences, so as to obtain accurate determinations of telomeric length or telomerase activity. In addition, compositions are provided for intracellular inhibition of telomerase activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/015.000; 435/091.100; 435/091.500; 536/024.330; 436/064.000; 935/077.000

L5 ANSWER 17 OF 28 USPATFULL
AN 95:1370 USPATFULL
TI Modulation of inflammatory responses by **administration** of GMP-140 or antibody to GMP-140
IN McEver, Rodger P., Oklahoma City, OK, United States
PA Board of Regents of the University of Oklahoma, Norman, OK, United States (U.S. corporation)
PI US 5378464 950103
AI US 89-320408 890308 (7)
DT Utility
EXNAM Primary Examiner: Walsh, Stephen G.
LREP Kilpatrick & Cody
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method using compounds inhibiting binding reactions involving GMP-140 to modulate an inflammatory response. The method is based on the discovery that GMP-140, released from the storage granules of platelets, endothelial cells, and megakaryocytes, and redistributed to the surface of the cells within seconds of activation by mediators such as thrombin, ionophores or histamine, binds to a ligand on neutrophils, and the plasma proteins C3b and protein S. Adhesion of the cells following activation is blocked directly by **administration** of antibody to GMP-140 or its ligand, or by competitive inhibition by **administration** of soluble GMP-140, the GMP-140 ligand, or the specific carbohydrate portion of the ligand bound by GMP-140.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/143.100
INCLS: 514/008.000

L5 ANSWER 18 OF 28 USPATFULL
AN 93:61009 USPATFULL
TI Antibodies to A4 amyloid peptide
IN Majocha, Ron, Wayland, MA, United States
Marotta, Charles A., Cambridge, MA, United States
Zain, Sayeeda, Pittsford, NY, United States
PA The McLean Hospital, Belmont, MA, United States (U.S. corporation)
University of Rochester, Rochester, NY, United States (U.S. corporation)
PI US 5231000 930727
AI US 91-733375 910722 (7)
RLI Continuation of Ser. No. US 87-105751, filed on 8 Oct 1987
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Cunningham, T.
LREP Sterne, Kessler, Goldstein & Fox
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Monoclonal** antibodies to a 28-mer peptide present within A4-amyloid are described. These antibodies exhibit unexpected specificity for amyloid plaque structures previously unrecognized in Alzheimer's disease brains. These **monoclonal** antibodies are useful as reagents for use in assays and imaging of A4-amyloid in Alzheimer's disease patients.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.100
INCLS: 435/007.200; 435/007.210; 435/240.270; 530/388.100; 436/501.000; 436/506.000

L5 ANSWER 19 OF 28 USPATFULL
AN 93:52495 USPATFULL
TI Method for transforming human B lymphocytes
IN Dalla-Favera, Riccardo, New York, NY, United States
Seremetis, Stephanie, New York, NY, United States
PA New York University, New York, NY, United States (U.S. corporation)
PI US 5223417 930629
AI US 91-790149 911108 (7)
RLI Continuation of Ser. No. US 89-340939, filed on 20 Apr 1989 which is a continuation-in-part of Ser. No. US 87-41803, filed on 23 Apr 1987, now patented, Pat. No. US 4997764 And a continuation-in-part of Ser. No. US 88-286680, filed on 19 Dec 1988, now abandoned
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner:

Cunningham, T.
LREP Darby & Darby
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 795
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed herein is a method for transforming human B-cells preferably by infecting them with Epstein-Barr virus followed by transforming the Epstein Barr virus infected cells with an activated human ras gene. The transformed cells are useful for producing human **monoclonal** antibodies either without further manipulation or after fusion with antibody-secreting cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/172.200
INCLS: 435/069.600; 435/070.210; 435/172.300; 435/240.270; 530/388.100; 530/808.000; 530/809.000; 935/093.000; 935/100.000

L5 ANSWER 20 OF 28 USPATFULL
AN 93:10613 USPATFULL
TI **Monoclonal** antibodies and antigen for human non-small cell lung carcinoma and other certain human carcinomas
IN Hellstrom, Karl E., Seattle, WA, United States
Brown, Joseph P., Seattle, WA, United States
Hellstrom, Ingegerd, Seattle, WA, United States
Marquardt, Hans, Mercer Island, WA, United States
PA Oncogen, Seattle, WA, United States (U.S. corporation)
PI US 5185432 930209
AI US 86-834172 860226 (6)
DT Utility
EXNAM Primary Examiner: Lacey, David L.; Assistant Examiner: Elliott, George C.
LREP Pennie & Edmonds
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 877
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is concerned with novel **monoclonal** antibodies which bind strongly to a protein antigen associated with human non-small cell lung carcinomas ("NSCLC") human small cell lung carcinomas and certain other human carcinomas including many carcinomas of the colon and breast. The antibodies bind to normal human cells to a much lesser degree than to tumor cells. The antibodies find use both in diagnostic methods such as the detection of malignant cells associated with NSCLC and in

therapeutic methods for treatment of human in NSCLC and certain other human carcinomas. Also disclosed is a novel 110,000 dalton glycoprotein antigen found on the cell surface of human non-small lung carcinoma tumor cells and on cells from certain other human cancers. The amino terminal amino acid sequence of this antigen is: ##STR1## in which X represents an unidentified amino acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/388.800
INCLS: 530/391.300; 435/240.270; 424/001.100

L5 ANSWER 21 OF 28 USPATFULL
AN 91:18881 USPATFULL
TI Transformation of human B-lympocytes with Epstein Barr virus and c-myc containing vectors
IN Dalla Favera, Ricardo, New York, NY, United States
PA New York University, New York, NY, United States (U.S. corporation)
PI US 4997764 910305
AI US 87-41803 870423 (7)
DT Utility
EXNAM Primary Examiner: Moskowitz, Margaret; Assistant Examiner: Kushan, Jeff
LREP Darby & Darby
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 542
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed herein is a method for transforming human B-cells by infecting them with Epstein Barr virus and transfecting the Epstein Barr virus infected cells with an activated human c-myc gene. The transformed cells are useful for producing human **monoclonal** antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/240.270
INCLS: 530/387.000; 530/809.000; 530/808.000; 530/828.000; 435/070.210; 435/069.600; 435/172.200; 435/172.300; 435/240.210; 435/240.200; 435/240.260; 435/320.100; 935/032.000; 935/034.000; 935/057.000; 935/071.000; 935/093.000; 935/100.000; 935/108.000; 935/109.000

L5 ANSWER 22 OF 28 USPATFULL
AN 90:50625 USPATFULL
TI Method for augmenting immune response
IN Cioco, Richard F., New York, NY, United States
Thorbecke, G. Jeanette, Douglaston, NY, United States
PA New York University, New York, NY, United States (U.S.

corporation)
PI US 4937071 900626
AI US 87-140911 871229 (7)
DCD 20070501
RLI Continuation of Ser. No. US 85-726089, filed on 23 Apr 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Teskin, Robin L.
LREP Darby & Darby
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 953
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for enhancing the ability for humoral immune response in a mammal comprising: exposing lymphocytes histocompatible with the lymphocytes of said mammal to the presence of delta-immunoglobulin at a concentration higher than that at which said lymphocytes would have been exposed while in the lymph or bloodstream of said mammal; and introducing said lymphocytes to the bloodstream or lymph of said mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.200
INCLS: 424/085.800; 424/086.000; 424/088.000; 435/029.000; 435/240.200; 530/380.000; 530/386.000; 530/387.000; 530/388.000; 436/513.000

L5 ANSWER 23 OF 28 USPATFULL
AN 90:48619 USPATFULL
TI Method of reducing tissue damage at an inflammatory site using a **monoclonal** antibody
IN Todd, III, Robert F., Ann Arbor, MI, United States
Simpson, Paul J., Ann Arbor, MI, United States
Lucchesi, Benedict R., Ann Arbor, MI, United States
Scholossman, Stuart F., Newton Centre, MA, United States
Griffin, James D., Sherborn, MA, United States
PA Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)
PI US 4935234 900619
AI US 88-165025 880307 (7)
DCD 20060620
RLI Continuation-in-part of Ser. No. US 87-61336, filed on 11 Jun 1987, now patented, Pat. No. US 4840793
DT Utility
EXNAM Primary Examiner: Draper, Garnette; Assistant Examiner: Kushan, Jeff
LREP Cass, Myron C.
CLMN Number of Claims: 10

ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 583
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of reducing tissue injury in humans or other animal species using a **monoclonal** antibody to inhibit specific phagocyte functions. The **monoclonal** antibody is selected to bind to phagocytic leukocytes for the purpose of inhibiting migration to an inflammatory site in the body and to inhibit the adhesion and spreading of activated leukocytes reaching such an area and then, block release of toxic substances by these cells. The **monoclonal** antibody is **administered** in vivo prior or early in the course of an experience leading to an injurious inflammatory response such as can result from restoration of myocardial blood flow interrupted by an acute coronary thrombosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.800
INCLS: 530/387.000; 530/388.000; 530/806.000; 530/808.000; 435/240.270

L5 ANSWER 24 OF 28 USPATFULL
AN 90:33921 USPATFULL
TI Method for augmenting immune response
IN Coico, Richard F., Larchmont, NY, United States
Thorbecke, G. J., Douglaston, NY, United States
PA New York University, New York, NY, United States (U.S. corporation)
PI US 4921667 900501
WO 8606490 861106
AI US 87-15074 870202 (7)
WO 86-US939 860423
870202 PCT 371 date
870202 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 85-726089, filed on 23 Apr 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Teskin, Robin L.
LREP Darby & Darby
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 960
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed is a method for enhancing the ability for humoral immune response in a mammal comprising:

exposing lymphocytes histocompatible with the lymphocytes of said

mammal to the presence of polymeric or aggregated delta-immunoglobulin at a concentration higher than that at which said lymphocytes would have been exposed while in the lymph or bloodstream of said mammal; and introducing said lymphocytes to the bloodstream or lymph of said mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.800
INCLS: 530/387.000; 530/389.000; 435/029.000; 435/240.200; 424/085.200; 424/095.000; 424/101.000

L5 ANSWER 25 OF 28 USPATFULL
AN 89:62856 USPATFULL
TI Antibodies to angiogenin: immunotherapeutic agents
IN Alderman, Edward M., Dedham, MA, United States
Fett, James W., Waltham, MA, United States
Vallee, Bert L., Brookline, MA, United States
PA President and Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)
PI US 4853219 890801
AI US 87-83231 870806 (7)
DT Utility
EXNAM Primary Examiner: Moskowitz, Margaret; Assistant Examiner: Kushan, Jeff P.
LREP Allegretti & Witcoff, Ltd.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 515
AB This invention relates to the production of antibodies to angiogenin or to fragments thereof and to methods of inhibiting angiogenesis in mammals by **administering** to mammals such antibodies or Fab fragments thereof so as to inhibit angiogenic activity. In addition, this invention relates to pharmaceutical compositions comprising therapeutically effective amounts of antibody that are immunologically reactive with angiogenin and which can be **administered** to inhibit angiogenesis.

INCL INCLM: 424/085.800
INCLS: 530/387.000; 530/395.000; 530/808.000; 530/809.000; 530/828.000; 530/399.000; 435/240.270; 935/104.000

L5 ANSWER 26 OF 28 USPATFULL
AN 89:49455 USPATFULL
TI Method of reducing tissue damage at an inflammatory site using a **monoclonal** antibody
IN Todd, III, Robert F., Ann Arbor, MI, United States
Lucchesi, Benedict R., Ann Arbor, MI, United States
Simpson, Paul J., Ann Arbor, MI, United States

Griffin, James D., Sherborn, MA, United States
Schlossman, Stuart F., Newton Centre, MA, United States
PA Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)
The University of Michigan, Ann Arbor, MI, United States (U.S. corporation)
PI US 4840793 890620
AI US 87-61336 870611 (7)
DT Utility
EXNAM Primary Examiner: Moskowitz, Margaret; Assistant Examiner: Kushan, Jeff P.
LREP Cass, Myron C.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 592
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of reducing tissue injury in humans or other animal species using a **monoclonal** antibody to inhibit specific phagocyte functions. The **monoclonal** antibody is selected to bind to phagocytic leukocytes for the purpose of inhibiting migration to an inflammatory site in the body and to inhibit the adhesion and spreading of activated leukocytes reaching such an area and then, block release of toxic substances by these cells. The **monoclonal** antibody is **administered** in vivo prior or early in the course of an experience leading to an injurious inflammatory response such as can result from restoration of myocardial blood flow interrupted by an acute coronary thrombosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.800
INCLS: 530/387.000; 530/380.000; 530/806.000; 435/240.270; 435/068.000

L5 ANSWER 27 OF 28 USPATFULL
AN 87:60237 USPATFULL
TI Human **monoclonal** antibodies against bacterial toxins
IN Insel, Richard A., Rochester, NY, United States
Gigliotti, Francis, Memphis, TN, United States
PA University of Rochester, Rochester, NY, United States (U.S. corporation)
PI US 4689299 870825
AI US 83-534658 830922 (6)
RLI Continuation-in-part of Ser. No. US 82-428747, filed on 30 Sep 1982, now abandoned
DT Utility
EXNAM Primary Examiner: Hazel, Blondel
LREP Pennie & Edmonds

CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1309
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The production of stable hybrid cell lines that secrete human **monoclonal** antibodies against bacterial toxins by fusing post-immunization human peripheral blood lymphocytes with nonsecretor mouse myeloma cells is described. Using the method, protective **monoclonal** antibodies against tetanus toxin and diphtheria toxin were produced that bind tetanus toxin and diphtheria toxin in vitro, respectively, and prevent tetanus and diphtheria in vivo in animals, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/240.270
INCLS: 435/172.200; 935/095.000; 935/096.000; 424/092.000; 530/387.000

L5 ANSWER 28 OF 28 USPATFULL
AN 84:11628 USPATFULL
TI Human nonsecretory plasmacytoid cell line
IN Ritts, Jr., Roy E., Rochester, MN, United States
PA Research Corporation, New York, NY, United States (U.S. corporation)
PI US 4434230 840228
AI US 81-292277 810812 (6)
DT Utility
EXNAM Primary Examiner: Wiseman, Thomas G.; Assistant Examiner: Tarcza, John Edward
LREP Scully, Scott, Murphy & Presser
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 641
AB A human non-secretory plasmacytoid continuous cell line, established for five years in more than 150 passages, is karyotypically normal, easily grown and has the characteristic features of a plasmablast excepting for its secretory defect, and can be used for the preparation of human-human hybridomas with human B-lymphocytes and separation of the resulting hybridomas from the plasmacytoma cell line by growth in CO.sub.2 -containing media, or by fluorescence activated cell sorting, or both.

INCL INCLM: 435/240.000
INCLS: 435/172.000; 435/948.000; 435/241.000

=> d his l6-; d 1-30 bib abs

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGB' ENTERED AT 14:26:23 ON 15 JAN 1999)

L6 587 S L3
L7 54 S L6 AND ADMIN?
L8 30 DUP REM L7 (24 DUPLICATES REMOVED)

L8 ANSWER 1 OF 30 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 1
AN 1998:451120 BIOSIS
DN PREV199800451120
TI Targeting of interleukin 2 to human ovarian carcinoma by fusion with a single-chain Fv of antifolate receptor antibody.
AU Melani, Cecilia (1); Figini, Mariangela; Nicosia, Daniela; Luison, Elena; Ramakrishna, Venkatesh; Casorati, Giulia; Parmiani, Giorgio; Eshhar, Zelig; Canevari, Silvana; Colombo, Mario P.
CS (1) Div. Experimental Oncol. "D", Istituto Nazionale Tumori, via Venezian 1, 20133 Milan Italy
SO Cancer Research, (Sept. 15, 1998) Vol. 58, No. 18, pp. 4146-4154. ISSN: 0008-5472.
DT Article
LA English
AB To provide a new tool for the immunotherapy of human ovarian carcinoma, we constructed a fusion protein between interleukin-2 (IL-2) and the single-chain Fv (scFv) of MOV19, a **monoclonal** antibody directed against alpha-folate receptor (alpha-FR), known to be overexpressed on human nonmucinous ovarian carcinoma. This was accomplished by fusing the coding sequences in a single open reading frame and expressing the IL-2/MOV19 scFv chimera under the control of the murine immunoglobulin kappa promoter in J558L **plasmacytoma** cells. The design allowed the construction of a small molecule combining the specificity of MOV19 with the immunostimulatory activity of IL-2. This might improve the tissue penetration and distribution of the fusion protein within the tumor, reduce its immunogenicity, and avoid the toxicity related to the systemic **administration** of IL-2. The IL-2/MOV19 fusion protein was stable on purification from the cell supernatant and was biologically active. Importantly, this construct was able to target IL-2 onto the surface of alpha-FR overexpressing tumor cells and stimulated the proliferation of the IL-2 dependent CTLL-2 cell line as well as that of human resting peripheral blood lymphocytes. In a syngeneic mouse model, IL-2/MOV19 scFv specifically targeted alpha-FR gene-transduced metastatic tumor cells without accumulating in normal tissues, due to its fast clearance from the body. Prolonged release of IL-2/MOV19 scFv by in vivo transplanted J558-EF6.1 producer cells protected 60% of mice from the development of lung metastases caused by an i.v. injection of alpha-FR gene-transduced tumor cells. Moreover, **treatment** with IL-2/MOV19 scFv, but not with recombinant IL-2, significantly

reduced the volume of s.c. tumors. The pharmacokinetics and biological characteristics of IL-2/MOV19 scFv might allow us to combine the systemic **administration** of this molecule with the adoptive transfer of in vitro retargeted T lymphocytes for the **treatment** of ovarian cancer, thereby providing local delivery of IL-2 without toxicity.

L8 ANSWER 2 OF 30 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 2
AN 1998:259730 BIOSIS
DN PREV199800259730
TI Irradiated IL-2 gene-modified plasmacytoma vaccines are more efficient than live vaccines.
AU Simova, Jana; Bubenik, Jan (1); Jandlova, Tana; Indrova, Marie
CS (1) Inst. Molecular Genetics, Acad. Sci. Czech Republic, Flemingovo nam. 2, 166 37 Prague 6 Czech Republic
SO International Journal of Oncology, (May, 1998) Vol. 12, No. 5, pp. 1195-1198.
ISSN: 1019-6439.
DT Article
LA English
AB The effect of irradiation on the **therapeutic** efficacy of IL-2 gene-modified **plasmacytoma** cells used as a vaccine in the immunotherapy of parental murine **plasmacytoma** X63-Ag8.653 was examined. Local **administration** of the IL-2-secreting **plasmacytoma** irradiated with a dose of 50 Gy inhibited i.p. **plasmacytoma** growth more effectively than the **administration** of non-irradiated, live cell vaccines. Whereas the vaccination with the live cell vaccine could substantially prolong the survival of the tumour-bearing mice but did not significantly induce tumour regressions, the irradiated vaccines could substantially increase the number of tumour-free animals. The irradiated vaccines produce higher amounts of IL-2 than the live cell vaccines both in vitro and in vivo. Depletion of CD4+ and CD8+ effector cells with **monoclonal** antibodies has significantly decreased the effect of the vaccination. It can be concluded that both, CD4+ and CD8+ T lymphocytes are required for effective IL-2 gene **therapy** of the X63-Ag8.653 **plasmacytoma** and that the higher effect of the irradiated vaccines is probably due to their higher IL-2 production.

L8 ANSWER 3 OF 30 PROMT COPYRIGHT 1999 IAC

AN 1998:284494 PROMT
TI Journal News . . . June 8 & 15, 1998 Reviews and Information From Periodicals and Journals Worldwide . . . Compiled by Alan D. Henderson
SO Vaccine Weekly, (8 Jun 1998) pp. N/A.
ISSN: 1074-2921.
LA English

WC 264
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Cancer Vaccines
Simova, J.; Bubenik, J.; Jandlova, T.; Indrova, M. "Irradiated IL-2 Gene-Modified Plasmacytoma Vaccines Are More Efficient Than Live Vaccines." International Journal of Oncology, May 1998;12(5):1195-1198.
According to the authors' abstract of an article published in International Journal of Oncology, "The effect of irradiation on the **therapeutic** efficacy of IL-2 gene-modified **plasmacytoma** cells used as a vaccine in the immunotherapy of parental murine **plasmacytoma** X63-Ag8.653 was examined. Local **administration** of the IL-2-secreting **plasmacytoma** irradiated with a dose of 50 Gy inhibited i.p. **plasmacytoma** growth more effectively than the **administration** of non-irradiated, live cell vaccines. Whereas the vaccination with the live cell vaccine could substantially prolong the survival of the tumour-bearing mice but did not significantly induce tumour regressions, the irradiated vaccines could substantially increase the number of tumour-free animals. The irradiated vaccines produce higher amounts of IL-2 than the live cell vaccines both in vitro and in vivo. Depletion of CD4(+) and CD8(+) effector cells with **monoclonal** antibodies has significantly decreased the effect of the vaccination. It can be concluded that both, CD4(+) and CD8(+) T lymphocytes are required for effective IL-2 gene **therapy** of the X63-Ag8.653 **plasmacytoma** and that the higher effect of the irradiated vaccines is probably due to their higher IL-2 production." The corresponding author for this study is: J Bubenik, Acad Sci Czech Republ, Inst Mol Genet, Flemingovo Nam 2, CR-16637 Prague 6, Czech Republic. For subscription information for this journal, contact the publisher: Int Journal Oncology, C, O Professor D a Spandidos, Editorial Office, 1, S Merkouri St, Athens 116 35, Greece.

L8 ANSWER 4 OF 30 PROMT COPYRIGHT 1999 IAC

AN 1998:264350 PROMT
TI Vaccine Development Simova, J.; Bubenik, J.; Jandlova, T.; Indrova, M. "Irradiated IL-2 Gene-Modified Plasmacytoma Vaccines Are More Efficient Than Live Vaccines." International Journal of Oncology, May 1998;12(5):1195-1198.
SO Vaccine Weekly, (1 Jun 1998) pp. N/A.
ISSN: 1074-2921.
LA English
WC 234
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB According to the authors' abstract of an article published in

International Journal of Oncology, "The effect of irradiation on the **therap utic** efficacy of IL-2 gene-modified **plasmacytoma** cells used as a vaccine in the immunotherapy of parental murine **plasmacytoma** X63-Ag8.653 was examined. Local **administration** of the IL-2-secreting **plasmacytoma** irradiated with a dose of 50 Gy inhibited i.p. **plasmacytoma** growth more effectively than the **administration** of non-irradiated, live cell vaccines. Whereas the vaccination with the live cell vaccine could substantially prolong the survival of the tumour-bearing mice but did not significantly induce tumour regressions, the irradiated vaccines could substantially increase the number of tumour-free animals. The irradiated vaccines produce higher amounts of IL-2 than the live cell vaccines both in vitro and in vivo. Depletion of CD4)+(and CD8)+(effector cells with **monoclonal** antibodies has significantly decreased the effect of the vaccination. It can be concluded that both CD4)+(and CD8)+()T lymphocytes are required for effective IL-2 gene **therapy** of the X63-Ag8.653 **plasmacytoma** and that the higher effect of the irradiated vaccines is probably due to their higher IL-2 production." The corresponding author for this study is: J Bubenik, Acad Sci Czech Republ, Inst Mol Genet, Flemingovo Nam 2, CR-16637 Prague 6, Czech Republic. For subscription information for this journal, contact the publisher: Int Journal Oncology, C, O Professor D a Spandidos, Editorial Office, 1, S Merkouri St, Athens 116 35, Greece.

L8 ANSWER 5 OF 30 MEDLINE DUPLICATE 3
AN 97239220 MEDLINE
DN 97239220
TI Therapeutic effect of cytomedicine on mesangio-proliferative glomerulonephritis in human interleukin-6 transgenic mice.
AU Okada N; Miyamoto H; Yoshioka T; Katsume A; Saito H; Yorozu K; Ueda O; Nakagawa S; Ohsugi Y; Mayumi T
CS Faculty of Pharmaceutical Sciences, Osaka University, Japan.
SO BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (1997 Mar) 20 (3) 255-8. Journal code: BPZ. ISSN: 0918-6158.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
EW 19970803
AB We previously demonstrated that IgG1 **plasmacytosis** in human interleukin-6 transgenic mice (hIL-6 Tgm) was suppressed by the implantation of SK2 hybridoma cells (SK2 cells, which secrete anti-hIL-6 **monoclonal** antibodies) microencapsulated in a semipermeable and biocompatible device. In this study, we demonstrated that the mesangio-proliferative glomerulonephritis in

hIL-6 Tgm was also improved by the same **treatment**. These results strongly support the concept of cytomedicine, which is a novel drug delivery system (DDS) using living cells. However, an electron microscopy study showed that cytomedicine has a limited duration of effectiveness because of the disappearance of space for cell proliferation in the microcapsule. Thus, the control of cell proliferation in a device must be developed to prolong the function and effectiveness of cytomedicine.

L8 ANSWER 6 OF 30 MEDLINE DUPLICATE 4
AN 97214660 MEDLINE
DN 97214660
TI Cytomedical **therapy** for IgG1 **plasmacytosis** in human interleukin-6 transgenic mice using hybridoma cells microencapsulated in alginate-poly(L)lysine-alginate membrane.
AU Okada N; Miyamoto H; Yoshioka T; Katsume A; Saito H; Yorozu K; Ueda O; Itoh N; Mizuguchi H; Nakagawa S; Ohsugi Y; Mayumi T
CS Faculty and Graduate School of Pharmaceutical Sciences, Osaka University, Japan.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1997 Feb 27) 1360 (1) 53-63. Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199706
EW 19970602
AB Cytomedical **therapy** for human interleukin-6 transgenic mice (hIL-6 Tgm) was implemented by the intraperitoneal injection of alginate-poly(L)lysine-alginate (APA) membranes microencapsulating SK2 hybridoma cells (APA-SK2 cells) which secrete anti-hIL-6 **monoclonal** antibodies (SK2 **mAb**). IgG1 **plasmacytosis** in the hIL-6 Tgm was suppressed by a single injection of APA-SK2 cells, and the survival time of these mice was remarkably prolonged. The viable cell number and the SK2 **mAb** -secretion of APA-SK2 cells increased for at least one month both under culture conditions and in allogeneic recipients (in vivo). Moreover, SK2 **mAb** which were secreted from APA-SK2 cells injected into allogeneic recipients was detected in serum at high concentrations; 3-5 mg/ml from day 14 to day 50 post-injection. In contrast, the injection of free SK2 cells had no **therapeutic** effect on hIL-6 Tgm. These results strongly suggest that APA membranes microencapsulating cells which were modified to secrete molecules useful for the **treatment** of a disorder were effective as an in vivo long-term delivery system of bioactive molecules, as 'cytomedicine'.

L8 ANSWER 7 OF 30 TOXLINE
AN 1997:59668 TOXLINE

DN CRISP-97-M03002-04
TI RISK FACTORS FOR IMMUNE MEDIATED ADVERSE EVENTS TO BIOLOGICS, FOODS, DEVICES.
AU MILLER F W
CS FDA
U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, .+-. S005
8
q +0.
NC Z01BM03002-04
SO (1996). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
DT (RESEARCH)
FS CRISP
LA English
EM 199705
AB RPROJ/CRISP Immune-mediated diseases appear to be increasing in prevalence in the population. These disorders are thought to be the result of chronic lymphocyte activation by selected environmental exposures in genetically susceptible individuals. The reasons for these reported increases in immune mediated diseases are unclear, although our increasing exposure to novel immune-altering biologics, foods, drugs, and devices may play a role in this phenomenon. We are investigating the pathogenesis, and environmental/genetic risk factors, that lead to these diseases that result in high morbidity and mortality. Specific investigations underway include: A. Immunogenetic risk factors for, and pathogenesis of, selected connective tissue and autoimmune diseases that develop following exposure to biologics, drugs, foods, and medical devices. Sera and cell banks, as well as large databases of clinical and genetic data, are being developed from idiopathic myositis patients, adult and pediatric, in order to compare the environmentally-related cases to this population and to gain an understanding of the natural history and disease assessment of these disorders. Preliminary data suggest that the myositis that develops after silicone implants differs from idiopathic myositis in clinical features, serology, and immunogenetics. Preliminary studies of the capsules surrounding explanted silicone mammary prostheses suggest that ongoing immune responses to silicone involve activation of macrophages, B cells and T lymphocytes via selected T cell receptor utilization. Preliminary animal studies suggest that the type and route of silicone **administration** greatly alters local and systemic immune responses and pathology. B. Pathogenesis of silicone-associated B lymphocyte activation. Silicone associated multiple myeloma (S-MM) and **monoclonal** gammopathy of undetermined significance (S-MGUS) are currently under investigation. As a result of our finding that some silicones induce **plasmacytomas** in genetically susceptible mice, we are evaluating the clinical features, immune responses and immunogenetics of S-MM and S-MGUS.

Searcher : Shears 308-4994

Two multi-center case-controlled studies are underway comparing either S-MM or S-MGUS patients with matched silicone controls and idiopathic MM or MGUS patients. C. Genetic risk factors for development of L-tryptophan-induced eosinophilia myalgia syndrome (EMS) are being studied. Preliminary data from case controlled exposure studies suggest that HLA DRB1 alleles determine risk for development of EMS and many of its sequelae. These studies have important implications in that immune-mediated adverse events to biologics, foods, drugs and devices are frequently the limiting factor in the development of novel **therapies** and vaccines. Better definition of genetic risk factors for these adverse events could lead to appropriate screening of populations that could prevent or minimize these adverse events.

L8 ANSWER 8 OF 30 MEDLINE DUPLICATE 5
AN 97013296 MEDLINE
DN 97013296
TI Multifocal plasmacytoma of hand and foot bones.
AU Antonijevic N; Radosevic-Radojkovic N; Colovic M; Jovanovic V; Rolovic Z
CS Institute of Haematology, Clinical Center of Serbia, Belgrade, Yugoslavia.
SO LEUKEMIA AND LYMPHOMA, (1996 May) 21 (5-6) 505-7.
Journal code: BNQ. ISSN: 1042-8194.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
EW 19970801
AB Simultaneous occurrence of localized **plasmacytomas** of both hands and feet has not been reported so far. Here we report a 40-year old female patient, who had at presentation pain and deformity. Of hands and feet, with numerous cystic lytic lesions of phalangeal, metacarpal and metatarsal bones, detected by X-rays. The biopsy of the affected bone showed moderately differentiated **plasmacytoma** of lambda light chain type (lambda-LC). Serum and urine biochemical analysis revealed the existence of lambda LC **monoclonal** component. The patient was **treated** by local radiotherapy and subsequent systemic chemotherapy, which consisted of 3 cycles of the M-2 protocol and 7 cycles of melphalan-prednisone. Five years after the diagnosis, the absence of **plasmacytoma** was confirmed by puncture biopsy of the left hand phalanx. **Monoclonal** protein in serum and urine was not detected.

L8 ANSWER 9 OF 30 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 95-24575 DRUGU P
TI Importance of TNF production for the curative effectiveness of low

dose melphalan therapy for mice bearing a large MOPC-315 tumor.

AU Gorelik L; Rubin M; Prokhorova A; Mokyr M B
CS Univ.Illinois
LO Chicago, Ill., USA

SO J.Immunol. (154, No. 8, 3941-51, 1995) 10 Fig. 41 Ref.
CODEN: JOIMA3 ISSN: 0022-1767

AV Department of Biochemistry (M/C 536), The University of Illinois at Chicago, 1819 West Polk Street, Chicago, IL 60612, U.S.A. (M.B.M.).

LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 95-24575 DRUGU P

AB Endogenous TNF was important for the therapeutic effectiveness of low dose melphalan (L-PAM, Sigma-Chem.) therapy in mice bearing a large MOPC-315 tumor. TNF was essential for the in-vitro generation of potent cytotoxic T lymphocyte activity by CD8+ T cells from L-PAM-treated tumor bearing mice. Positively selected Vbeta8+/CD8+ T cells derived from L-PAM tumor bearing mice produced large amounts of TNF upon antigenic stimulation and following adoptive transfer into MOPC-315 tumor bearers cured the mice in a TNF-dependent way. Mitomycin C was also used in these studies. Results indicate that low-dose L-PAM mediates its antitumor activity in mice bearing a large MOPC-315 tumor, at least in part, via TNF production which in turn promotes the generation of anti-MOPC-315 cytotoxic T lymphocyte activity.

ABEX Methods Female BALB/c mice (7-10-w-old) bearing a large tumor resulting from inoculation of MOPC-315 **plasmacytoma** cells 10 days earlier received L-PAM (1.5-2.5 mg/kg). Results **Administration** of hamster IgG anti-murine TNF **monoclonal** antibody greatly reduced the **therapeutic** effectiveness of low dose L-PAM. L-PAM **treatment** of tumor-bearing mice did not render the tumor cells more susceptible in-vitro to the cytotoxic effects of TNF. In-vitro exposure of tumor cells to TNF (100 ng/ml) did not reduce their tumorigenicity. TNF played a key role within the first 2 days of the generation of anti-MOPC-315 lytic activity by spleen cells from L-PAM-**treated** tumor bearing mice.MOPC-315 tumor cells were not sensitive to the cytotoxic effects of TNF before or after the chemotherapy. TNF added to the stimulation cultures of MOPC-315 tumor bearer spleen cells seemed to enhance the generation of antitumor cytotoxicity by CD8+ T cells in response to stimulation with MOPC-315 tumor cells in an antigen-specific manner. TNF was important for the ability of Vbeta8+/CD8+ T cells from L-PAM-**treated** tumor-bearing mice to mediate tumor eradication in-vivo upon adoptive transfer. (W81/LF)

L8 ANSWER 10 OF 30 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 6
AN 1996:64276 BIOSIS

DN PREV199698636411
TI Oral low-dose etoposide therapy for refractory multiple myeloma with extramedullary involvement.
AU Kato, Yoshiro (1); Takeda, Hiroyuki; Mihara, Hidetsugu; Kobayashi, Hideo; Kamijima, Sinsuke; Kuwahara, Mika; Oguri, Takashi; Nagasaka, Tetsuro
CS (1) Second Dep. Intern. Med., Aichi Med. Coll., 21 Yazako Karimata Nagakute-cho, Aichi-gun, Aichi 480-11 Japan
SO Internal Medicine (Tokyo), (1995) Vol. 34, No. 10, pp. 1023-1026. ISSN: 0918-2918.
DT Article
LA English
AB A 65-year-old man was hospitalized with IgG kappa-type multiple myeloma (MM) and enormous subcutaneous **plasmacytomas**. Two different combination chemotherapy regimens (MMCP and AVPP) and alpha-interferon **therapy** were ineffectual. Oral **administration** of etoposide at 50 mg/day was subsequently started, the tumors completely disappeared after 5 months. The blood level of **monoclonal** protein became undetectable after 8 months of continuous **treatment**. The side effect noted was loss of hair. The course in this patient suggests that long-term daily low-dose **administration** of etoposide should be attempted in patients with refractory MM and extramedullary **plasmacytoma**.

L8 ANSWER 11 OF 30 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 7
AN 1994:438995 BIOSIS
DN PREV199497451995
TI Radioimmunotherapy of nude mice bearing a human interleukin 2 receptor alpha-expressing lymphoma utilizing the alpha-emitting radionuclide-conjugated **monoclonal** antibody 212Bi-anti-Tac.
AU Hartmann, Frank; Horak, Eva M.; Garmestani, Kayhan; Wu, Chuanchu; Brechbiel, Martin W.; Kozak, Robert W.; Tso, J.; Kosteiny, Sheri A.; Gansow, Otto A.; Nelson, David L.; Waldmann, Thomas A. (1)
CS (1) Metabolic Branch, Natl. Cancer Inst., Build. 10, 4N115, NIH, Bethesda, MD 20892 USA
SO Cancer Research, (1994) Vol. 54, No. 16, pp. 4362-4370. ISSN: 0008-5472.
DT Article
LA English
AB The efficacy, specificity, and toxicity of bismuth (212Bi) alpha particle-mediated radioimmunotherapy was evaluated in nude mice bearing a murine lymphoma transfected with the human CD25 (human Tac; interleukin 2 receptor alpha (IL-2R-alpha)) gene. The **therapeutic** agent used was the tumor-specific humanized **monoclonal** antibody anti-Tac conjugated to 212Bi. The human IL-2R-alpha-expressing cell line was produced by transfecting the gene encoding human Tac into the murine **plasmacytoma** cell

line SP2/0. The resulting cell line, SP2/Tac, expressed approximately 18,000 human IL-2R-alpha molecules/cell. Following s.c. or i.p. injection of 2 times 10-6 SP2/Tac cells into nude mice, rapidly growing tumors developed in all animals after a mean of 10 and 13 days, respectively. The bifunctional chelate cyclohexyldiethylenetriaminepentaacetic acid was used to couple 212Bi to the humanized anti-Tac **monoclonal** antibody. This immunoconjugate was shown to be stable in vivo. Specifically, in pharmacokinetic studies in nude mice, the blood clearance patterns of i.v. **administered** 205/206Bi-anti-Tac and coinjected 125I-anti-Tac were comparable. The toxicity and **therapeutic** efficacy of 212Bi-anti-Tac were evaluated in nude mouse ascites or solid tumor models wherein SP2/Tac cells were **administered** either i.p. or s.c., respectively. The i.p. **administration** of 212Bi-antiTac, 3 days following i.p. tumor inoculation, led to a dose-dependent, significant prolongation of tumor-free survival. Doses of 150 or 200 mu-Ci prevented tumor occurrence in 75% (95% confidence interval, 41-93%) of the animals. In the second model, i.v. **treatment** with 212Bi-anti-Tac 3 days following s.c. tumor inoculation also resulted in a prolongation of the period before tumor development. However, prevention of tumor occurrence decreased to 30% (95% confidence interval, 11-60%). In both the i.p. and s.c. tumor trials, 212Bi-anti-Tac was significantly more effective for i.p. (P2 = 0.0128 50/100 mu-Ci 212Bi-anti-Tac versus 50/100 mu-Ci Mik-beta; P2 = 0.0142 150/200 mu-Ci anti-Tac versus 150/200 mu-Ci Mik-beta) and for s.c. tumors (P2 = 0.0018 100,uCi anti-Tac versus 100 mu-Ci Mik-beta; P2 = 0.0042 200 mu-Ci anti-Tac versus 200 mu-Ci Mik-beta-1) than the control antibody Mik/beta-1 coupled to 212Bi at comparable dose levels. In contrast to the efficacy observed in the adjuvant setting, **therapy** of large, established s.c. SP-2/ Tac-expressing tumors with i.v. **administered** 212Bi-anti-Tac (at doses up to 200 mu-Ci/animal) failed to induce tumor regression. Pharmacokinetic and tissue distribution studies of radiolabeled anti-Tac in this particular **therapeutic** situation provided an explanation for this observation. Only 5-6% of the injected dose of radiolabeled antibody was present per g o tumor at 2 h following injection at a time when 75% of the **administered** 212Bi radioactivity had decayed. Furthermore, at this time point, there was no greater uptake of Bi-anti-Tac into Tac-expressing tumors than wa observed with Tac-nonexpressing variants of SP2/0. Finally, the specific antibody 205/206Bi-anti-Tac was not enriched in the tumor when compare to the irrelevant **monoclonal** antibody 205/206Bi-Mik-beta-1. Although specific enrichment of radiolabeled Bi-anti-Tac was not seen at 2 h, such enrichment in the tumor was observed at 5 and 24 h postinjection with up to 15.6% injected dose present per g of tumor. The dose-limiting acute toxicity following i.v. **administration** of 212Bi-anti-Tac was bone marrow suppression, which was observed at doses above 200 mu-Ci. In

summary, 212Bi-anti-Tac as a complete antibody may be of only limited value in the **therapy** of bulky solid tumors due to the short physical half-life of 212Bi and the time required to achieve a useful tumor:normal tissue ratio of the radionuclide following **administration** of the radiolabeled antibody. However, this radionuclide may be useful in select situations such as adjuvant or intracavitary **therapy**, strategies that target the vascular endothelial cells of tumors, or in the **treatment** of leukemias.

L8 ANSWER 12 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 94302355 EMBASE
TI Inhibition of interleukin-6 (IL-6): A new approach for the **therapy** of human **plasmacytomas**?.
AU Klein B.; Bataille R.
CS Institute for Molecular Genetics, Montpellier, France
SO LEUKEMIA, (1994) 8/9 (1607-1608).
ISSN: 0887-6924 CODEN: LEUKED
CY United Kingdom
DT Journal
FS 016 Cancer
025 Hematology
037 Drug Literature Index
LA English

L8 ANSWER 13 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 8
AN 93318552 EMBASE
TI Involvement of TCR-V.beta.8.3+ cells in the cure of mice bearing a large MOPC-315 tumor by low dose melphalan.
AU Mokyr M.B.; Rubin M.; Newell K.A.; Prokhorova A.; Bluestone J.A.
CS Department of Biochemistry, University of Illinois, PO Box 6998, Chicago, IL 60680, United States
SO J. IMMUNOL., (1993) 151/9 (4838-4846).
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal
FS 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB We have previously shown that the curative efficacy of low dose melphalan (L-phenylalanine mustard; L-PAM) for mice bearing a large s.c. MOPC-315 tumor requires the participation of CD8+ (but not CD4+) T cell-dependent antitumor immunity. Here we show that CD8+ T cells obtained from regressing tumors on day 4 or 5 after low dose L-PAM **therapy** of MOPC-315 tumor bearers (L-PAM TuB mice) display a preferential enhancement in the utilization of the

TCR-V.beta.8.3 gene segment as compared to CD8+ T cells from normal lymph nodes. **Treatment** of L-PAM TuB mice with **mAb** F23.1, which leads to the depletion of V.beta.8.3+ cells, as well as V.beta.8.1 and 8.2+ cells, led to a significant reduction in the ability of their tumor-infiltrating lymphocytes as well as their spleen cells to lyse MOPC-315 tumor cells in vitro in a short term assay. In addition, the **mAb** F23.1 **treatment** almost completely abrogated the lytic activity of the tumor-infiltrating lymphocytes against another syngeneic, antigenically related **plasmacytoma** (the MOPC-104E). Moreover, the **mAb** F23.1 **treatment** significantly reduced the curative effectiveness of low dose L-PAM for mice bearing a large MOPC-315 tumor. In contrast, **mAb** KJ16 **treatment**, which leads to the depletion of V.beta.8.1 and 8.2+ cells (but not V.beta.8.3+ cells), did not reduce significantly the curative effectiveness of low dose L-PAM for such MOPC-315 tumor bearers. Thus, V.beta.8.3+ T cells are important for the curative effectiveness of low dose L-PAM **therapy** for MOPC- 315 tumor bearers, and it is conceivable that the V.beta.8.3+ cells mediate their effect (at least in part) by contributing to the acquisition of CTL activity against **plasmacytoma**-shared Ag.

L8 ANSWER 14 OF 30 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 93-28116 DRUGU P
TI An In Vivo Model of Human Multidrug-Resistant Multiple Myeloma in SCID Mice.
AU Bellamy W T; Odeleye A; Finley P; Huizenga B; Dalton W S; Weinstein R S
LO Tucson, Arizona, United States
SO Am.J.Pathol. (142, No. 3, 691-98, 1993) 3 Fig. 1 Tab. 26 Ref.
CODEN: AJPAA4 ISSN: 0002-9440
AV Department of Pathology, University of Arizona, 1501 N. Campbell Avenue, Tucson, AZ 85724, U.S.A. (8 authors).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 93-28116 DRUGU P
AB An in-vivo model of human multiple myeloma was established in severe combined immunodeficient (SCID) mice using the RPMI-8226 human myeloma cell-line and the p-glycoprotein expressing multidrug-resistant (MDR) 8226/C1N subline. Xenograft take, as evidenced by overt **plasmacytomas**, was more successful after i.p. than after i.v. or s.c. **administration**. Tumor take and burden were also assessed by immunophenotyping and urinary **monoclonal** human lambda light chain excretion. I.p. doxorubicin (DOX, Sigma-Chem.) markedly reduced human Ig urinary excretion and increased survival time in mice with drug-sensitive

8226 tumors, but not those with the MDR variant, 8226/C1N. The model will be useful in the evaluation of new **therapeutic** approaches to MDR myeloma and chemosensitizers of PGP-mediated MDR.

ABEX Methods SCID BALBc/C.17 mice (aged 5-8 wk) received human 8226 (10-50 million) or 8226/C1N (10 million) cells by an i.p., s.c. or i.v. route and i.p. DOX 1-75 mg/kg bolus, 0.1-2.5 mg/kg every 2 days or 1.5-7 mg/kg every 4 days from day 21. Results The 8826 line required 50 million cells compared to only 10 million for the 8226/C1N line to achieve 100% xenograft take. Although no tumors were visible at autopsy at 2-4 wk, a dose of 10-25 million 8226 cells led to increasing human lambda light chain expression. S.c. xenografts took rarely and there were no i.v. takes. All untreated tumor-bearers died (mean survival time 42.3 days with 10 million 8226/C1N cells, 45.9 days with 25 million 8226 cells and 45.4 days with 50 million 8226 cells) and showed weight and fur loss. Plasmacytomas were mostly on the peritoneum and in the perinephric fat, were invasive into the psoas muscle and diaphragm and metastasized to the liver, kidneys, pancreas, prostate and testicles. Tumors were human lambda light chain-positive and kappa light chain-negative. Excretion of human lambda light chain by tumor-bearers was detected at day 5 and increased linearly for at least 30 days. The maximum tolerated dose of DOX was 2 mg/kg every 4 days. At 1.5 mg/kg every 4 days, DOX reduced the level of human lambda light chain in the urine and increased the survival time of 8226, but not 8226/C1N-bearing mice. (K10/SAB)

L8 ANSWER 15 OF 30 MEDLINE DUPLICATE 9
AN 92328544 MEDLINE
DN 92328544
TI Multiple primary cutaneous plasmacytomas.
AU Green T; Grant J; Pye R; Marcus R
CS Department of Dermatology, Addenbrooke's Hospital, Cambridge, England..
SO ARCHIVES OF DERMATOLOGY, (1992 Jul) 128 (7) 962-5. Ref: 20
Journal code: 6WU. ISSN: 0003-987X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199210
AB BACKGROUND--Cutaneous **plasmacytoma** is an uncommon tumor and is mostly seen in the context of end-stage multiple myeloma. Only 20 cases of primary cutaneous **plasmacytoma** have been documented. A significant proportion of these patients went on to develop systemic disease with a poor prognosis. In a number of patients, however, the abnormal clone of plasma cells may arise in the skin and never progress to multiple myeloma involving the bone

marrow. OBSERVATIONS--We describe a patient who developed multiple primary cutaneous **plasmacytomas** after a possible insect bite reaction. The **monoclonality** of the tumor cells is demonstrated using immunohistochemical techniques. He has been **treated** vigorously with chemotherapy and local radiotherapy and remains well 3 years after diagnosis. Bone marrow has been harvested for use as an autologous bone marrow transplant in the event of systemic relapse. CONCLUSIONS--Unlike previous reports of this rare entity, this case documents the **monoclonality** of tissue plasma cells with immunohistochemical techniques. As cutaneous **plasmacytomas** have been reported with an early significant mortality, unlike extramedullary **plasmacytomas** elsewhere, we have advocated combination chemotherapy and cryopreservation of uninvolved bone marrow for future autologous bone marrow transplantation should systemic myelomatosis develop in the patient.

L8 ANSWER 16 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 91341671 EMBASE
TI Multiple myeloma: A review of 92 cases at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia.
AU Khalil S.H.; Padmos A.; Ernst P.; Clink H.M.
CS Department of Pathology, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia
SO ANN. SAUDI MED., (1991) 11/6 (642-646).
ISSN: 0256-4947 CODEN: ANSMEJ
CY Saudi Arabia
DT Journal
FS 005 General Pathology and Pathological Anatomy
016 Cancer
025 Hematology
037 Drug Literature Index
LA English
SL English; Arabic
AB A review of 92 cases of multiple myeloma (66 males and 26 females) seen at the King Faisal Specialist Hospital and Research Centre from October 1975 through December 1987 revealed the age for affected patients ranged from 23 to 90 years (mean, 56 years). Six percent of the patients were less than 40 years old at the time of diagnosis. Bone pain was the most common presenting symptom in our patients (80%), most frequently involving the back. Anemia was the initial finding in 74%, followed by **plasmacytoma** (22.8%), hypercalcemia (19.6%), and renal insufficiency (18.5%). Skeletal survey abnormalities were seen in 92.4% of the cases, with osteolytic lesions as the predominant finding. Serum protein electrophoresis showed a **monoclonal** paraprotein in 78% of the cases, of which 55.5% were the IgG class. Free light chains were detected in the urine of 20 patients. The median survival time for all patients was 68 months. Twenty patients died of renal failure

and/or infection. The combination of melphalan and prednisone was used for **treatment** in 37 patients, while 31 patients received the M2 protocol and 19 patients received different **therapy** such as VCEP (vindesine, cyclophosphamide, VP 16 and prednisone), MPV (melphalan, prednisone, and vincristine) or high-dose melphalan. Five patients either refused **treatment** or died before **treatment** could be started.

L8 ANSWER 17 OF 30 MEDLINE DUPLICATE 10
AN 91363055 MEDLINE
DN 91363055
TI A case of Crow-Fukase syndrome associated with idiopathic thrombocytopenic purpura.
AU Kawaguchi Y; Nagasato K; Yoshimura T; Motomura M; Tsujihata M; Nagataki S
CS First Department of Internal Medicine, Nagasaki University School of Medicine, Japan..
SO NO TO SHINKEI. BRAIN AND NERVE, (1991 Apr) 43 (4) 377-80. Journal code: AR5. ISSN: 0006-8969.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 199112
AB A 40-year-old man was admitted to our hospital because of paresthesia and weakness of the limbs. At the age of 38, he was diagnosed as having an idiopathic thrombocytopenic purpura (ITP) which have been refractory to oral **administration** of prednisolone and splenectomy. Platelet-associated IgG was elevated markedly at that time. It was, however, only mildly elevated on this admission. He showed polyneuritis, generalized pigmentation, hirsutism, and marked edema on the legs. The bone X-ray disclosed a lytic lesion in the left iliac bone, which was confirmed as a **plasmacytoma** by bone biopsy. Axonal degeneration with marked loss of myelinated figure was seen on sural nerve biopsy. Serum immunoelectrophoresis revealed his **monoclonal** IgG was lambda type. Then, he was diagnosed as having a Crow-Fukase syndrome associated with ITP. Plasma exchange, pulse **therapy**, and irradiation to **plasmacytoma** resulted in a slight improvement of the polyneuritis and the skin symptoms, and a disappearance of edema. However, ITP has not responded to these **therapies**. Although the same autoimmune mechanism is suggested in these conditions, we could not clarify how this **monoclonal** IgG produce both polyneuritis and ITP.

L8 ANSWER 18 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 91137481 EMBASE
TI Case report: Marked plasmacytosis and immunoglobulin abnormalities following infusion of streptokinase.

AU Gorden L.; Smith C.; Graber S.E.
CS Department of Medicine, VA Medical Center, 1310 24th Avenue South, Nashville, TN 37212, United States
SO AM. J. MED. SCI., (1991) 301/3 (186-189).
ISSN: 0002-9629 CODEN: AJMSA
CY United States
DT Journal
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
AB Marked **plasmacytosis** is an uncommon clinical finding associated with plasma cell dyscrasias and certain reactive states, particularly serum sickness. Moreover, serum sickness-like reactions are a well-recognized complication of **therapy** with streptokinase. In this report, the authors describe a patient who developed a transient, but striking, **plasmacytosis** and an unexplained fever following streptokinase **treatment** for a pulmonary embolus. An evaluation for multiple myeloma was completely negative except for the occurrence of serum **monoclonal** -like proteins which largely disappeared over an eight month period.

L8 ANSWER 19 OF 30 MEDLINE DUPLICATE 11
AN 90123468 MEDLINE
DN 90123468
TI Early induction of immune resistance against leukemia in lethally total body irradiated mice reconstituted with syngeneic bone marrow cells obtained from previously immunized donor mice.
AU Skorski T; Kawalec M; Kawiak J
CS Department of Cytophysiology, Medical Center of Postgraduate Education, Warsaw, Poland..
SO BONE MARROW TRANSPLANTATION, (1990 Jan) 5 (1) 23-7.
Journal code: BON. ISSN: 0268-3369.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199005
AB BALB/c x DBA/2 F1 (CD2F1) mice were lethally irradiated and reconstituted with syngeneic bone marrow cells (SBMC) obtained from normal or previously immunized (against L1210 lymphatic leukemia) donors. These recipient mice are called TBI + SBMT or TBI + Imm-SBMT mice, respectively. TBI + Imm-SBMT, but not TBI + SBMT mice, were able to develop strong immune resistance against L1210 leukemia, but not against MOPC 104E **plasmacytoma**, if the immunization procedure (four i.p. injections at weekly intervals of immunogenic L1210 cells) was started as early as 7 days posttransplantation.

Searcher : Shears 308-4994

Incubation of Imm-SBMC with mafosfamide (ASTA Z7654) before grafting abrogated the ability of the recipient mice to develop early resistance against the leukemia. **Treatment** of Imm-SBMC with **monoclonal** or polyclonal antibodies plus complement showed that two or three subpopulations of Imm-SBMC were necessary for the transfer of immune information against leukemia: T lymphocytes with phenotype Thy 1.2+, Lyt 1+2-, I-Ad-, macrophages with phenotype Mac-1+, I-Ad-, and probably asialo-GM 1+ cells. Recipient mice immunized against L1210 leukemia before TBI + SBMT do not develop early resistance to the leukemia.

L8 ANSWER 20 OF 30 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 89-38237 DRUGU P
TI Enhancement of the Effectiveness of Lyt - 2 + T-Cells for Adoptive Chemoimmunotherapy by Short-Term Exposure of Tumor-Bearer Spleen Cells to Polyethylene Glycol and/or Melphalan.
AU Wise J A; Mokyr M B; Dray S
LO Chicago, Illinois, United States
SO Cancer Res. (49, No. 13, 3613-19, 1989) 6 Tab. 41 Ref.
CODEN: CNREA8 ISSN: 0008-5472
AV Department of Microbiology and Immunology (M/C 790), Box 6998, Chicago, IL 60680, U.S.A. (S.D.).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 89-38237 DRUGU P
AB Tumor-infiltrated spleen cells (TISC) from mice bearing s.c. MOPC-315 **plasmacytomas** cultured with inactivated MOPC-315 stimulator cellsacquired some effectiveness in curing mice bearing a nonpalpable MOPC-315 tumor that had been **treated** with a subcurative dose of i.p. cyclophosphamide (CY, Cytoxan, Mead-Johnson). The effectiveness was enhanced if PEG (BDH) was added to the culture. Lyt 2 = cells were responsible for the effectiveness and inclusion of PEG increased their number. The effectiveness was enhanced further by pretreatment of TISC with melphalan (MP, Wellcome).
ABEX Methods Female BALB/c mice (6-8 wk) were injected with 1000000 MOPC-315 cells on day 0; 4 days later they received CY (10 mg/kg). Donor spleen cells were **administered** i.v. on day 5. Spleen cells were cultured with MOPC-315 stimulator tumor cells and 2% w/v PEG-6000. Results The cure rate for mice injected with TISC cultured in the presence of MPOC-315 and PEG was 92.1% vs. 45.2% MOPC-315 alone. 20.1% PEG alone and 9.5% control. The cure rate with TISC cultured with MOPC-315 and PEG was 68.4% vs. 16.7% MOPC-315 alone. Spleen cells obtained from mice 10 days after inoculation with tumor cells (tumor 22 mm) were optimally effective (92% cure). By day 13 when animals were at terminal stages of tumor progression their spleen cells became less

effective (29% cure). The cure rate obtained with spleen cells taken at day 13 (tumor 20 mm) from mice injected with a smaller number of cells initially was 91%. Depletion of T-cells or subsets by treatment with **monoclonal** antibodies and complement indicated that the Lyt 2 + T cells and not L3T4 + T cells were responsible for the effectiveness of the cultured TISC. The L3T4 + T cells were not required during culture of TISC for generation of Lyt 2 + cells. TISC cultured with MOPC-315 and PEG contained almost twice the number of Lyt 2 + cells as did those cultured without PEG. However, increasing the number of Lyt 2 + T cells in the absence of PEG did not have the same effect. Culturing TISC with MP (0.5 nmol/ml) increased the cure rate to 82.3% vs. 51.7% MOPC-315 and PEG alone. (W140/JW)

L8 ANSWER 21 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 89210082 EMBASE
TI Successful in vitro graft-versus-tumor effect against an Ia-bearing tumor using cyclosporine-induced syngeneic graft-versus-host disease in the rat.
AU Geller R.B.; Esa A.H.; Beschorner W.E.; Frondoza C.G.; Santos G.w.; Hess A.D.
CS Johns Hopkins Oncology Center, Baltimore, MD 21205, United States
SO BLOOD, (1989) 74/3 (1165-1171).
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal
FS 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
LA English
AB Lethally irradiated LouM rats reconstituted with syngeneic bone marrow and then **treated** with cyclosporine (CsA) for 40 consecutive days following transplant developed a graft-v-host disease (GVHD)-like syndrome after CsA cessation. This model of GVHD was used to define and characterize a graft-v-tumor (GVT) effect against a syngeneic **plasmacytoma** CRL1662 cell line which expresses class II major histocompatibility (MHC) antigen (Ia). Nylon wool-nonadherent spleen cells from animals who developed syngeneic GVHD were capable of significant lysis against chromium-labeled tumor target cells in a four-hour chromium released cell mediated lympholysis assay; maximum lysis occurred five days following cessation of CsA when clinical signs first appeared. Cytolytic activity declined to baseline as GVHD symptoms resolved. Fractionation of splenocytes into lymphocyte subsets demonstrated that cytolytic lymphocytes (CTLs) of the OX8 phenotype (non-helper T) were capable of significant lysis against tumor target cells. Lysis of tumor cells was blocked by preincubation with **monoclonal** antibodies (**MoAb**) specific for the rat anti-class II MHC antigen but not with **MoAb** against class

I. Incubation of tumor cells with gamma-interferon increased expression of tumor class II MHC antigens and significantly increased their susceptibility to lysis by nylon wool-nonadherent splenocytes from animals with syngeneic GVHD. These studies have demonstrated an in vitro GVT of syngeneic GVHD against an Ia-bearing tumor; the effector cell is a CTL of the OX8 phenotype specific for the class II MHC antigen.

L8 ANSWER 22 OF 30 JICST-EPlus COPYRIGHT 1999 JST
AN 890431069 JICST-EPlus
TI Refractory IgA-multiple myeloma successfully treated with a combination therapy of VAD and interferon-.ALPHA.: A case report.
AU OMURA MINORU; MUTA KOICHIRO; NATORI SHOICHI; SUEMATSU EIICHI; NISHIMURA JUNJI; NAWATA HAJIME
CS Kyushu Univ., Faculty of Medicine
SO Kyushu Ketsueki Kenkyu Doko Kaishi (Journal of Kyushu Hematological Society), (1988) vol. 36, no. 1/2, pp. 39-43. Journal Code: Y0673A (Fig. 2, Tbl. 1, Ref. 12)
ISSN: 0451-1611
CY Japan
DT Journal; Article
LA Japanese
STA New
AB A 56-year-old female was admitted to our hosopital because of visual disturbance and general fatigue. Examinations of admission showed severe anemia(Hb. 4.2g/dl), an increase in serum IgA(8036mg/dl), serum **monoclonal** protein(IgA..KAPPA.), and .KAPPA. type urinary Bence-Jones protein. Bone marrow aspiration revealed atypical **plasmacytosis**(25.9%) and thus the diagnosis of IgA-multiple myeloma was made. Though she underwent an ordinary chemotherapy with alkylating agents and plasmapheresis, the level of **monoclonal** protein was unchanged. Therefore, a combination **therapy** of VAD(adriamycin(ADR) 10mg/day, vincristine(VCR) 0.4mg/day, dexamethasone(Dexa) 40mg/day) and interferon-.ALPHA. were given. After two cource of the **treatment**, following a rapid reduction in the level of serum IgA, anemia and clinical symptoms were dramatically improved. The literatural aspects of VAD **treatment** are also discussed.(author abst.)

L8 ANSWER 23 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 87142935 EMBASE
TI Nonsecretory multiple myeloma.
AU Rubio-Felix D.; Giralt M.; Pilar Giraldo M.; et al.
CS Servicio Regional de Hematologia-Hemoterapia, 'Hospital Miguel Servet', 50009 Zaragoza, Spain
SO CANCER, (1987) 59/10 (1847-1852).
CODEN: CANCAR
CY United States
FS 005 General Pathology and Pathological Anatomy

006 Internal Medicine
016 Cancer
025 Hematology
LA English
AB Among 186 patients with multiple myeloma (MM), five women were diagnosed as having MM without M-component in serum and or urine at the diagnosis and along the evolution. Bone marrow **plasmacytosis** at greater than 30% was found in all patients and bone x-rays showed lytic lesions in all but one case, osteoporosis in all, and pathologic fractures in two. Serum electrophoresis showed a striking hypogammaglobulinemia in all, and polyclonal immunoglobulin levels were markedly reduced. The immunofluorescence of plasma cells in bone marrow was positive for **monoclonal** light chain polypeptides in four patients, and the ultrastructure showed mature plasmocytes with a wide rough endoplasmic reticulum (RER) and an intact Golgi apparatus. In three patients, **therapy** with melphalan plus prednisone was started. The remaining two were **treated** with an M-2 protocol. Death was an early event in two patients; the response was good in the remaining patients, without differences regarding secretory MM. Despite some reports stressing an unfavorable prognosis in MM without M-component, in our series it is roughly the same as in MM with secretion.

L8 ANSWER 24 OF 30 MEDLINE DUPLICATE 12
AN 88148645 MEDLINE
DN 88148645
TI [Polyneuropathy and solitary bone plasmacytoma. A new case]. Polyneuropathie et plasmocytome solitaire osseux. Une nouvelle observation.
AU Lanoe Y; Delauche M C; Amarenco G; Durieux M; Toledano D; Bitar Z; Goudal H
CS Service de Neurologie, C. H. G. R. Ballanger, Aulnay-sous-Bois..
SO ANNALES DE MEDECINE INTERNE, (1987) 138 (7) 498-501. Ref: 36
Journal code: 5FZ. ISSN: 0003-410X.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 198806
AB The authors report a case of acute polyneuropathy revealing a solitary osseous **plasmacytoma** with osteo-dense and osteolytic bone lesions. Initially, the rapid progression of the sensory and motor loss led to **treatment** by plasma exchanges and irradiation of the **plasmacytoma**. Four months later, despite a significant improvement of the neurological condition, serum protein electrophoresis continued to show a peak of

monoclonal immunoglobulin. Chemotherapy with cyclophosphamide and prednisone was **administered** for one year whilst the neuropathy continued to regress. This case, which presents many classical features of plasma cell dyscrasia (polyneuropathy with albumino-cytological dissociation, radiological osseous condensation, low concentrations of lambda light chain protein), illustrates some unusual features of solitary **plasmacytomas** associated with peripheral neuropathy: the young age of our patient, an acute progression of the neuropathy in the early stages, tumoral localisation in the diaphysis of a long bone.

L8 ANSWER 25 OF 30 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 87-18110 DRUGU P T E S
TI Iododerma Occurring After Orally **Administered** Iopanoic Acid.
AU Boudoulas O; Siegle R J; Grimwood R E
LO Columbus, Ohio, United States
SO Arch.Dermatol. (123, No. 3, 387-88, 1987) 1 Fig. 13 Ref.
CODEN: ARDEAC ISSN: 0003-987X
AV 456 Clinic Dr, Room 4731, Columbus, OH 43210, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 87-18110 DRUGU P T E S
AB A case of iododerma after oral cholecystography with iopanoic acid (Telepaque, Sterling-Winthrop) in a 45-yr-old man with multiple myeloma is reported. Iododerma was treated with prednisone. Multiple myeloma was treated with vincristine sulfate, melphalan, cyclophosphamide, prednisone and vincristine, carmustine, doxorubicin HCl, and prednisone for remission induction therapy.
ABEX A 45-yr-old man presented with a 2-wk history of an eruption on his face, neck, trunk, and extremities. The patient had taken 6 iopanoic acid tablets for an oral cholecystogram twice within a wk. 2 Days after the last dose, he developed a skin eruption, which had been steadily worsening since then. A physical examination disclosed multiple 0.05- to 2-cm vesiculopustular, vegetating, nodular lesions, with ulceration predominantly on the face, neck, and trunk. There were a few scattered lesions on the extremities. A skin biopsy specimen obtained from a back lesion stained with hematotoxylin-eosin showed acute inflammatory cells, primarily polymorphonuclear leukocytes, which were present in the dermis with areas demonstrating focal karyorrhexis. The epidermis was acanthotic, with an ulceration present on the margin of the specimen. The diagnosis of acute iododerma was made. The patient was started on 40 mg of prednisone daily. There was a 50% clearing of the skin lesions in 1 wk. Multiple myeloma was diagnosed on the basis of the presence of a **monocloncal** gammopathy (IgG),

Bence Jones protein in the urine greater than 100 mg/d, reduced serum IgM and IgA levels, and 15% **plasmacytosis** of the bone marrow. **Treatment** for the multiple myeloma consisted of vincristine sulfate, melphalan, cyclophosphamide, prednisone and vincristine, carmustine, doxorubicin hydrochloride, and prednisone for remission induction **therapy**. Over 3 wk, the skin lesions completely resolved. The most recent examination 6 wk after the initiation of **therapy** disclosed only postinflammatory hyperpigmentation. (PBD) (R.E.G.)

L8 ANSWER 26 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 85240449 EMBASE
TI Multiple myeloma in a child.
AU Bernstein S.C.; Perez-Atayde A.R.; Weinstein H.J.
CS Division of Pediatric Hematology and Oncology, Dana-Farber Cancer Institute, Boston, MA 02115, United States
SO CANCER, (1985) 56/8 (2143-2147).
CODEN: CANCAR
CY United States
LA English
AB A 12-year-old girl with the diagnosis of multiple myeloma is described. She presented with a nasopharyngeal mass which was histologically found to be a **plasmacytoma**. Serum immunoelectrophoresis revealed an IgA-kappa M-protein (4.9 g/dl). There were approximately 20% atypical plasma cells in a bone marrow biopsy specimen. The diagnosis was further supported by immunohistochemical demonstration of cytoplasmic **monoclonal** IgA-kappa in the tumor cells of both the nasopharyngeal and bone marrow biopsies. The patient was **treated** with chemotherapy for 1 year, at which time she became refractory to **treatment** , based on serum IgA levels. Five months after cessation of **therapy**, she continues to exhibit a significant objective response, remaining clinically well with a stable, elevated serum IgA level.

L8 ANSWER 27 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 84111472 EMBASE
TI Suppression of antitumor immunity by macrophages in spleens of mice bearing a large MOPC-315 tumor.
AU Ye Q.W.; Mokyr M.B.; Pyle J.M.; Dray S.
CS Department of Microbiolgy and Immunology, University of Illinois at Chicago, Health Sciences Center, Chicago, IL 60612, United States
SO CANCER IMMUNOL. IMMUNOTHER., (1984) 16/3 (162-169).
CODEN: CIIMDN
CY Germany, Federal Republic of
LA English
AB We had shown previously that progression of MOPC-315 **plasmacytoma** growth is associated with an increase in the percentage of macrophages in the spleen as well as a decrease in the

ability of tumor-bearer spleen cells to mount an antitumor cytotoxic response upon in vitro immunization. Here we provide evidence that macrophages in the MOPC-315 tumor-bearer spleen are responsible at least in part for the suppression of the generation of antitumor cytotoxicity. Accordingly, removal of most macrophages by depletion of phagocytic cells or Sephadex G-10-adherent cells from spleens of mice bearing a large tumor resulted in augmented antitumor immune potential. Also, Sephadex G-10-adherent spleen cells from tumor-bearing (but not normal) mice drastically suppressed the in vitro generation of antitumor cytotoxicity by normal spleen cells. The suppressive activity of these adherent cells did not reside in contaminating suppressor T cells, since it was not reduced by **treatment** with **monoclonal** anti-Thy 1.2 antibody plus complement. The Sephadex G-10-adherent cell population from the tumor-bearer spleen suppressed the in vitro generation of antitumor cytotoxicity against autochthonous tumor cells but not against allogeneic EL4 tumor cells, and hence the suppression was apparently specific. The suppressive activity of the Sephadex G-10-adherent cell population from tumor-bearer spleens was overcome by **treatment** of the tumor-bearing mice with a low curative dose of cyclophosphamide. This immunomodulatory effect of a low dose of the drug in overcoming the suppression mediated by the Sephadex G-10-adherent cell population enables the effector arm of the immune system of tumor-bearing mice to cooperate effectively with the drug's tumoricidal activity in tumor eradication.

L8 ANSWER 28 OF 30 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 83-31976 DRUGU T
TI Pseudoerythrocytosis in Myeloma with Associated Peripheral Neuropathy.
AU Lockhart S P; Phaure T A J
LO Stafford, United Kingdom
SO Postgrad.Med.J. (59, No. 690, 266-68, 1983) 8 Ref.
CODEN: PGMJAO ISSN: 0032-5473
AV Department of Haematology, Staffordshire General Infirmary, Foregate Street, Stafford, England.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 83-31976 DRUGU T
AB In a youth who presented with a prednisolone **treated** peripheral neuropathy associated with pseudoerythrocytosis in myeloma (initially a solitary **plasmacytoma**, secreting IgG-lambda), **treatment** of his plasma cell neoplasia afforded some neurological improvement. Such **treatment** included radiotherapy and **administration** of prednisolone, melphalan and cyclophosphamide.
ABEX A 19-yr-old male presented with a 6-mth history of symmetrical

sensorimotor peripheral neuropathy, mainly affecting the lower limbs with moderate quadriceps weakness. At age 9 yr, he had received rifampicin, isoniazid and PAS for pulmonary tuberculosis. He was on no medication at presentation. Raised hemoglobins and elevated platelet counts were noted. Action potentials of sensory nerves and motor conduction velocities were reduced, with muscle biopsy revealing changes consistent with denervation and partial reinnervation. Prednisolone (60 mg/day for 1 wk, tapering to zero over the next 8 mth) had little effect on the neuropathy, which progressed significantly for 4 mth after presentation. He developed a **plasmacytoma**, further characterized by immunoelectrophoresis to be producing a **monoclonal** IgG-lambda band in serum and small amounts of lambda-light chain in 100 x concentrated urine. The raised hemoglobin was due to a pseudoerythrocytosis. His plasma cell tumor (in the upper right femur) responded well to initial radiotherapy (regional irradiation with 4 krad over 20-day) with a 5-day course of melphalan during a tapering prednisolone regimen (lasting 1 mth). Some 8 mth later, hemoglobin and platelets had both become elevated again, necessitating commencement on pulsed cyclophosphamide + prednisolone. After another 6 mth, both neoplastic and neurologic indicators showed significant improvement. **Treatment** was continued.

L8 ANSWER 29 OF 30 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 84-01099 BIOTECHDS
TI **Monoclonal** antibody for the protection of neonatal pigs and calves from toxic diarrhea;
construction of a hybridoma secreting **monoclonal** antibody (conference paper)
AU Sadowski P L; Acres S D; Sherman D M
CS Mol.Genetics
LO Molecular Genetics, Inc., Minnetonka, Minnesota 55343, U.S.A.
SO Basic Life Sci.; (1983) 25, 93-99
CODEN: BLFSBY
DT Journal
LA English
AN 84-01099 BIOTECHDS
AB **Monoclonal** antibody technology which allows the unlimited production of antibody with defined specificity has resulted in renewed interest in passive immunization as a **treatment** alternative for disease. Purified pilus protein from enteropathogenic Escherichia coli strain K99 was used to immunize Balb/c mice and spleen cells from hyperimmunized mice were fused with cells of a P3-NS-1-Ag 4/1 **plasmacytoma**. Hybridomas producing antibody reacting with the K99 pilus were identified using an ELISA. The K99-reactive **monoclonal** antibody specificity was characterized by immunoprecipitation studies and the ability of the antibody to protect newborn pigs and calves from

death due to strain K99 was determined. The antibody was found to be efficacious in protection of the animals when **administered** orally. (19 ref)

L8 ANSWER 30 OF 30 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 80041936 EMBASE
TI Chemotherapy in the management of extramedullary plasmacytoma.
AU Wiltshaw E.
CS Roy. Marsden Hosp., London SW3 6JJ, United Kingdom
SO CANCER CHEMOTHER. PHARMACOL., (1978) 1/3 (167-175).
CODEN: CCPHDZ
CY Germany, Federal Republic of
LA English
AB The results of chemotherapy in 24 patients with extramedullary **plasmacytoma** are reported. Complete regressions, including disappearance of **monoclonal** paraprotein and healing of bone lesions, were seen in 12 of 20 (60%) patients with disseminated disease. Extrameullary **plasmacytoma** responds better to chemotherapy than myeloma, and **treatment** should be pursued with vigour until all signs of disease have disappeared. Sensitivity to single-agent chemotherapy may vary, and if **treatment** fails with one agent, others should be tried.

=> d his l9- ful; d 1-29 .beverly

(FILE 'CAPLUS' ENTERED AT 14:47:35 ON 15 JAN 1999)
L9 17475 SEA ABB=ON PLU=ON (INTERLEUKIN OR IL)(W)6 OR IL6 OR (B(1W)(DIFFERENTIAT? OR STIMULAT?) OR HYBRIDOM? OR HEPATOCYTE)(2W)FACTOR
L10 693 SEA ABB=ON PLU=ON L9(5A)(DISEAS? OR DISORDER)
L11 54 SEA ABB=ON PLU=ON L10 AND (MOAB OR MAB OR MONOCLON? OR (PMI OR PM1 OR PM(W)(1 OR I))(W)ANTIBOD? OR BP2998 OR BP 2998)
L12 13 SEA ABB=ON PLU=ON L11 AND ADMIN?
L13 13 SEA ABB=ON PLU=ON L12 NOT L3
L14 131 SEA ABB=ON PLU=ON L10(S)(TREAT? OR THERAP?)
L15 22 SEA ABB=ON PLU=ON L14 AND (MOAB OR MAB OR MONOCLON? OR (PMI OR PM1 OR PM(W)(1 OR I))(W)ANTIBOD? OR BP2998 OR BP 2998)
L16 16 SEA ABB=ON PLU=ON L15 NOT (L3 OR L13)
L17 29 SEA ABB=ON PLU=ON L12 OR L16

L17 ANSWER 1 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1998:685492 CAPLUS
DN 129:301329
TI Treatment of autoimmune diseases by inhibition of cytokine signal transduction
SO Nippon Naika Gakkai Zasshi (1998), 87(9), 1745-1750

CODEN: NNGAAS; ISSN: 0021-5384
AU Nishimoto, Norihiro; Yoshizaki, Kazuyuki; Kishimoto, Tadamitsu
PY 1998
AB A review with 20 refs., on (1) pathogenesis of autoimmune diseases, (2) a variety of physiol. functions of IL-6, (3) involvement of IL-6 in the pathogenesis of Castleman's disease (CD), lupus nephritis, and rheumatoid arthritis (RA), (4) treatment of CD and RA with humanized **monoclonal** antibodies against IL-6 receptor, and (5) future prospects of the therapy of autoimmune diseases by inhibiting cytokine signal transduction.

L17 ANSWER 2 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1998:568725 CAPLUS
DN 129:198859
TI Primers for detection of Kaposi's sarcoma-associated herpesvirus by PCR and diagnosis and treatment of multiple myeloma and **monoclonal** gammopathy
SO PCT Int. Appl., 137 pp.
CODEN: PIXXD2
IN Berenson, James R.; Rettig, Matthew B.; Vescio, Robert A.

APPLICATION NO.	DATE
WO 98-US2820	19980212
AU 98-61644	19980212

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9835684	A2	19980820	WO 98-US2820	19980212
WO 9835684	A3	19981203		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9861644	A1	19980908	AU 98-61644	19980212

PY 1998
1998
1998
AB Methods for the detection and identification of Kaposi's sarcoma-assocd. herpesvirus (KSHV)-specific nucleic acids or proteins in biol. samples derived from patients diagnosed with multiple myeloma (MM) or **monoclonal** gammopathy of undetd. significance (MGUS) are described. The virus may also be a diagnostic or **therapeutic** target in other **interleukin** 6-dependent **disease**. KSHV nucleic acids are detected in patients using PCR or RT-PCR of cell

or tissue samples. MM or MGUS may then be treated prophylactically or therapeutically using anti-sense DNA or antibodies to the virus or antiviral chemotherapy (no data). The detection of the virus in non-malignant bone marrow stromal cells of MM and MGUS patients is demonstrated.

L17 ANSWER 3 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1998:520259 CAPLUS
DN 129:135115
TI Experimental mucosal induction of uveitis with the 60-kDa heat shock protein-derived peptide 336-351
SO Eur. J. Immunol. (1998), 28(8), 2444-2455
CODEN: EJIMAF; ISSN: 0014-2980
AU Hu, Wei; Hasan, Adam; Wilson, Amanda; Stanford, Miles Richard; Li-Yang, Yun; Todryk, Steven; Whiston, Roy; Shinnick, Thomas; Mizushima, Yutaka; Van der Zee, Ruurd; Lehner, Thomas
PY 1998
AB S.c. immunization of rats with the human 60-kDa heat shock protein (HSP)-derived peptide 336-351 induced clin. and/or histol. uveitis in 80% of rats. Subsequent expts. to prevent the development of uveitis by oral or nasal **administration** of the peptide have failed. Instead, uveitis was induced in 74.6% of rats given the peptide orally (5 times), in 75% given the peptide nasally (5 times) or 91.7% of those **administered** the peptide by both routes (10 times). Histol. examn. showed that any one route of **administration** of the peptide elicited iridocyclitis in 42.2% but loss of photoreceptors only in 4.9% of rats. In contrast, sequential **administrations** of the peptide by a combined mucosal-s.c. route resulted in iridocyclitis in only 25% but loss of photoreceptors in 40% of animals. Examn. of mRNA from CD4-enriched splenic cells by reverse transcription-PCR failed to yield differences in Th1 or Th2 cytokines. Treatment with **monoclonal** antibody (**mAb**) to CD4 yielded a dose-dependent decrease in uveitis from 82% to 25%. Similarly, treatment with IL-4 decreased the development of uveitis from 68% to 30.4%. Treatment of the rats with **mAb** to CD8 greatly enhanced the onset of uveitis (from about 22 days in the controls to 11 days) and all the rats developed uveitis by day 24. Thus, CD4+ cells mediate, whereas CD8+ cells suppress the development of uveitis. The authors suggest that this novel exptl. mucosal model of induction of uveitis by the human 60-kDa HSP-derived peptide 336-351, which is specific in stimulating T cell responses in Behcet's disease, is consistent with the oro-genital onset of this disease and the development of uveitis.

L17 ANSWER 4 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1998:427003 CAPLUS
DN 129:188255
TI IL-6 receptor blockage inhibits the onset of autoimmune kidney

disease in NZB/WF1 mice
SO Clin. Exp. Immunol. (1998), 112(3), 397-402
CODEN: CEXIAL; ISSN: 0009-9104
AU Mihara, M.; Takagi, N.; Takeda, Y.; Ohsugi, Y.
PY 1998
AB Here, the authors examd. the preventive effect of anti-mouse IL-6 receptor (IL-6R) antibody, MR16-1, on the development of autoimmune kidney disease in female NZB/W F1 (BWF1) mice. Immunol. tolerance to MR16-1 or isotype-matched control antibody, KH-5, was induced by the simultaneous **administration** of anti-CD4 **MoAb** in mice. Thereafter, mice were i.p. given 0.5 mg of MR16-1, 0.5 mg of KH-5, or saline once a week from 13 to 64 wk of age. MR16-1 treatment dramatically suppressed proteinuria and prolonged the survival time of BWF1 mice. Only 1 out of 10 mice died with high levels of proteinuria throughout the expt. MR16-1 almost completely suppressed the prodn. of IgG forms of anti-DNA and anti-TNP antibodies, but not the IgM forms of these antibodies. In particular, all IgG subclasses (IgG1, IgG2a, IgG2b, and IgG3) of anti-DNA antibody prodn. were suppressed. Moreover, serum IgG1, IgG2a, and IgG3 levels in MR16-1-treated mice were lower than those in saline- and KH-5-treated mice, whereas serum IgM and IgA levels were not influenced. Thus, MR16-1 potently suppressed the development of autoimmune disease in BWF1 mice, and this was attributed to its effect of specific suppression of IgG class antibody prodn.

L17 ANSWER 5 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1998:381874 CAPLUS
DN 129:135048
TI The effect of .gamma..delta. T cell depletion on cytokine gene expression in experimental allergic encephalomyelitis
SO J. Immunol. (1998), 160(12), 5955-5962
CODEN: JOIMA3; ISSN: 0022-1767
AU Rajan, Alice J.; Klein, Jonathan D. S.; Brosnan, Celia F.
PY 1998
AB In exptl. autoimmune encephalomyelitis (EAE), a model for multiple sclerosis, we showed previously that depletion of .gamma..delta. T cells using the **mAb** GL3 immediately before disease onset, or during the chronic phase, significantly ameliorated clin. severity. We now report on the effect of .gamma..delta. T cell depletion on expression of five cytokine genes, IL-1, IL-6, TNF, lymphotoxin, and IFN-.gamma. in spinal cords of mice during the pe-onset, onset, height, and recovery phases of EAE, and on expression of type II nitric oxide synthase. In control animals, the mRNAs for IL-1 and IL-6 rose dramatically at disease onset and peaked before disease height, whereas the mRNAs for TNF, lymphotoxin, and IFN-.gamma. rose more slowly and peaked with peak of disease. In GL3-treated animals, a dramatic redn. in all five cytokines was noted at disease onset, but only IFN-.gamma. remained

significantly reduced at a time point equiv. to height of disease in control animals. ELISA data confirmed the reduced levels of IL-1 and **IL-6** at **disease** onset in GL3-**treated** animals, and pathol. anal. demonstrated a significant redn. in both mRNA and protein expression at the height of disease in GL3-**treated** animals. These results suggest that .gamma..delta. T cells contribute to the pathogenesis of EAE by regulating the influx of inflammatory cells into the spinal cord and by augmenting the proinflammatory cytokine profile of the inflammatory infiltrates.

L17 ANSWER 6 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1998:89360 CAPLUS
DN 128:166368
TI The interleukin 6 of human herpesvirus 8 and its use in diagnostics and therapeutics
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
IN Fleckenstein, Bernhard; Albrecht, Jens-Christian; Neipel, Frank; Friedman-Kien, Alvin; Huang, Yao-Qi

	APPLICATION NO.	DATE
AI	WO 96-EP3199	19960719

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9803657	A1	19980129	WO 96-EP3199	19960719

W: US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PY 1998
AB Human herpesvirus 8 is found to carry a gene for an interleukin 6 that can bind to the interleukin 6 receptor. The interleukin and the gene encoding can be used in the diagnosis and treatment of a no. of diseases including: Kaposi sarcoma, Castleman's disease, multiple myeloma, kidney cell carcinoma, mesangial proliferative glomerulonephritis or B cell lymphoma. The protein may be manufd. by expression of the cloned gene.

L17 ANSWER 7 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1998:1580 CAPLUS
DN 128:87883
TI AGP-1: a new member of the tumor necrosis factor family
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
IN Johnson, Merrie J.; Simonet, William S.; Danilenko, Dimitry M.

	APPLICATION NO.	DATE
AI	WO 97-US9895	19970606
	AU 97-33810	19970606

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9746686	A2	19971211	WO 97-US9895	19970606
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9733810	A1	19980105	AU 97-33810	19970606

PY 1997
1998

AB A novel member of the tumor necrosis factor (TNF) family was identified and obsd. to be involved in inflammation and necrosis, esp. of the liver, myelopoiesis and bone resorption. The polypeptide is termed AGP-1. Nucleic acid sequences, vectors and host cells for the expression of AGP-1 are disclosed. Methods for identifying antagonists of AGP-1, pharmaceutical compns. comprising AGP-1 and methods of treatment using AGP-1 and AGP-1 antagonists are also disclosed. Liver-specific expression of the mouse cDNA from the ApoE promoter in transgenic mice led to alterations in the gross anatomy of the (enlarged, friable, and tan-colored) and increased levels of serum bilirubin, alk. phosphatase, alanine aminotransaminase and aspartate aminotransferase. There was also marked periportal inflammation and bile duct hyperplasia. Peritoneal inflammation was also found.

L17 ANSWER 8 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1997:722421 CAPLUS
DN 128:33031
TI Modulation of chronic excessive interleukin-6 production in multiple myeloma does not affect thyroid hormone concentrations
SO Metab., Clin. Exp. (1997), 46(11), 1343-1348
CODEN: METAAJ; ISSN: 0026-0495
AU van Zaanen, H. C. T.; Romijn, J. A.; Sauerwein, H. P.; Lokhorst, H. M.; Warnaar, S. O.; Aarden, L. A.; Endert, E.; van Oers, M. H. J.
PY 1997
AB Interleukin-6 (IL6) is believed to be involved in alterations of thyroid hormone metab. in acute non-thyroidal illness. To evaluate the effects of IL6 on thyroid hormone metab. in a chronic **IL6**-mediated **disease**, the authors measured thyroid hormone concns. in multiple myeloma patients **treated** with i.v. anti-IL6 chimeric **monoclonal** antibodies ([cMabs] Kd = 6.25.times.10-12 mol/L). Twelve patients were studied, receiving at least one complete treatment cycle of 14 days (daily dose: 5 mg, 10 mg, 20 mg, and 40 mg). Eight of them also completed a second treatment cycle of 14 days. Thyroid hormone concns. were measured

before, during, and after treatment with the anti-IL6 cMab. Even in the group with the lowest dosage, IL6 activity measured by the B9 bioassay was blocked completely. Compared with the ref. ranges, 10 of 12 patients had one or more abnormal pretreatment values for thyroid hormone concns. Thyroid autoantibodies were neg. in all patients. There was no correlation between thyroid hormone concns. and IL6 levels, although plasma IL6 levels were increased in all but one subject. Moreover, neutralization of free IL6 by the anti-IL6 cMab did not affect thyroid hormone concns., although IL6-dependent C-reactive protein (CRP) levels decreased to undetectable levels in 11 of 12 patients. Two patients developed infectious complications resulting in increased free IL6 and CRP levels and in profound alterations of thyroid hormone levels consistent with an acute euthyroid sick syndrome. The authors conclude that IL6 is not a major determinant of thyroid hormone abnormalities in a chronic disease like multiple myeloma, but IL6 may be involved in thyroid hormone metab. in acute diseases (probably in combination with other factors).

L17 ANSWER 9 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1997:651840 CAPLUS
DN 127:330078
TI Safety and kinetic properties of a humanized antibody to human interleukin-6 receptor in healthy non-human primates
SO Toxicology (1997), 122(3), 163-170
CODEN: TXCYAC; ISSN: 0300-483X
AU Shinkura, Hirofumi; Imazeki, Ikuo; Fukushima, Naoshi; Chiba, Nobuyuki; Takahashi, Fumiaki; Aikawa, Hitoshi; Kitamura, Hidetomo; Furuichi, Tastuya; Horiba, Naoshi; Ohsugi, Yoshiyuki
PY 1997
AB A **monoclonal** antibody, hPM-1, was constructed by grafting the complementarity detg. regions to human interleukin-6 (IL-6) receptor, raised in mouse, onto a human antibody backbone (humanized antibody). It is expected to be useful as a therapeutic agent for **IL-6**-related **diseases** such as multiple myeloma. To investigate the toxicol. and kinetic properties of hPM-1 preliminarily, normal cynomolgus monkeys, which showed cross-reactivity with hPM-1, were i.v. **administered** with hPM-1 at doses of 0 (vehicle), 4, or 40 mg/kg once a week for 13 wk. Upon toxicol. examn., there were no changes in clin. signs, food consumption, body wts., urinalysis, body temps., electrocardiograms, hematol. and biochem. parameters including blood platelet counts, serum levels of IgG and C-reactive protein, and pathol. findings. In a kinetic study, serum concns. of hPM-1 showed a linearity between doses of 4 and 40 mg/kg. The serum concns., even at a dose of 4 mg/kg, were maintained at a high enough level to inhibit the IL-6 functions throughout the period of the study. Concns. of hPM-1 in bone marrow were almost equal to those in serum. The antibodies against hPM-1 were detected only in 1 of 4 monkeys receiving hPM-1.

Thus, blockage of the IL-6 receptor by hPM-1 does not induce any influence on a healthy living body, and hPM-1 is not toxic under the conditions of this investigation.

L17 ANSWER 10 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1997:561367 CAPLUS
DN 127:219430
TI Role of interleukin-6 in the paraneoplastic inflammatory syndrome associated with renal-cell carcinoma
SO Int. J. Cancer (1997), 72(3), 424-430
CODEN: IJCNAW; ISSN: 0020-7136
AU Blay, Jean-Yves; Rossi, Jean-Francois; Wijdenes, John; Menetrier-Caux, Christine; Schemann, Stephane; Negrier, Sylvie; Philip, Thierry; Favrot, Marie
PY 1997
AB The authors investigated the possible causative role of interleukin 6 (IL-6) in the paraneoplastic inflammatory syndrome and in paraneoplastic cholestasis (Stauffer syndrome) assocd. with renal-cell carcinoma in a series of 119 patients with metastases. IL-6 levels were found significantly higher in patients with paraneoplastic fever and wt. loss. Patients with detectable serum IL-6 (76%) had significantly higher serum CRP, haptoglobin, and serum alk.-phosphatase and .gamma.-glutamyltransferase levels. Platelets, polymorphonuclear neutrophil (PMN) and monocyte counts were also significantly higher in patients with detectable serum IL-6; in contrast, Hb levels were significantly lower in patients with serum IL-6 over 80 pg/mL. Three of these patients were included in a phase-II trial of an anti-IL-6 **monoclonal** antibody given daily during 21 days. Redns. of CRP, haptoglobin and serum alk. phosphatases were obsd. in all 3 patients during anti-IL-6 **administration**, with a subsequent increase up to or above pre-treatment levels after the end of anti-IL-6. Decrease of platelets, PMN and monocyte counts were also obsd. in the 3 patients during anti-IL-6 **administration**, with a normalization of cell counts in a patient with increased platelets, PMN and monocyte counts. Hb concn., serum albumin concn. and lymphocyte counts remained stable in the 3 patients during and after anti-IL-6 **administration**. Serum IL-6, as evaluated by IRMA, decreased in the 3 patients during anti-IL-6 **administration**, but increased above pre-treatment levels after the end of anti-IL-6 **administration**. These results demonstrate that IL-6 is involved in the physiopathol. of paraneoplastic syndromes obsd. in patients with metastatic renal-cell carcinoma, in particular CRP and haptoglobin increase, paraneoplastic cholestasis, also paraneoplastic thrombocytosis, neutrophilia and monocytosis.

L17 ANSWER 11 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1997:209359 CAPLUS

DN 126:275981
TI The therapeutic potential of interleukin-6 hyperagonists and antagonists
SO Expert Opin. Invest. Drugs (1997), 6(3), 237-266
CODEN: EOIDER; ISSN: 0967-8298
AU Kallen, Kari-Josef; Meyer zum Buschenfelde, Karl-Hermann; Rose-John, Stefan
PY 1997
AB A review with 284 refs. Interleukin-6 (IL-6) is a 4-helical protein that binds to a specific IL-6 receptor on target cells and to two mols. of the promiscuous signal transducing protein, glycoprotein 130 (gp130). Structure-function anal. has led to the definition of mol. contacts between IL-6 and its receptor subunits. This knowledge has led to the design of competitive antagonistic proteins that retain their receptor binding capability, but fail to stimulate one or both gp130 proteins; the properties of such recombinant antagonistic proteins are compared with traditional neutralizing **monoclonal** antibodies targeted at IL-6 or receptor subunits. Furthermore, several strategies have been employed to construct mols. with increased bioactivity. Possible **therapeutic** applications in putative **IL-6** dependent hematol. **disorders**, e.g., Castleman's disease (CD), POEMS syndrome, multiple myeloma, and bone diseases, e.g., Paget's disease, osteoporosis, are outlined. IL-6 antagonists could also, in theory, suppress inflammatory activity in rheumatic and autoimmune diseases and could prevent secondary amyloidosis. This principle may prove advantageous in myocardial infarction (MI) and unstable angina pectoris. More generally, IL-6 antagonists could improve the wasting and microcytic anemia of chronic diseases. IL-6 antagonists might slow down development of mesangioproliferative glomerulonephritis (MPGN). Hyperagonistic variants of IL-6 have a potential use in the ex vivo expansion of hematopoietic progenitor cells and as thrombopoietic agents. They might well be the first drugs to aid liver regeneration in vivo.

L17 ANSWER 12 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1996:423442 CAPLUS
DN 125:84468
TI Critical involvement of interferon gamma in the pathogenesis of T-cell activation-associated hepatitis and regulatory mechanisms of interleukin-6 for the manifestations of hepatitis
SO Hepatology (Philadelphia) (1996), 23(6), 1608-1615
CODEN: HPTLD9; ISSN: 0270-9139
AU Mizuhara, Hidekazu; Uno, Maki; Seki, Nobuo; Yamashita, Masakatsu; Yamaoka, Makiko; Ogawa, Toshikazu; Kaneda, Kenji; Fujii, Takashi; Senoh, Hachiro; Fujiwara, Hiromi
PY 1996
AB A single i.v. injection of Con A induces T-cell activation and an acute hepatitis in mice. This study investigated the role of

interferon .gamma. (IFN-.gamma.) in the pathogenesis of this hepatitis model. Striking increases in the plasma levels of various cytokines, including tumor necrosis factor (TNF), interleukin-2 (IL-2), and IFN-.gamma., were detected before the increase in plasma aminotransferase levels induced by Con A injection. TNF levels peaked within 2 h, whereas IFN-.gamma. levels peaked at 6 h after Con A injection. In contrast to a sharp peak of TNF levels, high IFN-.gamma. levels were detected for a more prolonged period. Passive immunization with anti-IFN-.gamma. **monoclonal** antibody (**MAb**) conferred a dose-dependent protection against liver injury in this model. This protection was obsd. when anti-IFN-.gamma. **MAb** was **administered** at least 30 min before Con A injection but not when given 1 h after Con A injection. The protection from Con A-induced hepatitis was also induced by **administration** of rIL-6 before Con A injection. RIL-6 treatment induced significant albeit incomplete inhibition of IFN-.gamma. and TNF prodn., whereas this regimen did not affect IL-2 prodn. Despite striking protective effects of rIL-6 or anti-IFN-.gamma. **MAb**, comparable levels of cellular (both T cell and polymorphonuclear cell) infiltration were detected in liver sections from animals untreated, or treated with either rIL-6 or anti-IFN-.gamma. **MAb**. Moreover, electron microscopic examn. showed that infiltrating T cells exhibited a blastoid appearance in all groups. Thus, IFN-.gamma. plays a crit. role in the development of Con A-induced acute hepatitis and IL-6 **administration** can regulate the manifestation of hepatitis through mechanisms including the reduced prodn. of inflammatory cytokines such as IFN-.gamma..

L17 ANSWER 13 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1996:69410 CAPLUS
DN 124:143399
TI **Administration** of neutralizing antibodies to interleukin-6 (IL-6) reduces experimental autoimmune encephalomyelitis and is associated with elevated levels of IL-6 bioactivity in central nervous system and circulation
SO Mol. Med. (Cambridge, Mass.) (1995), 1(7), 795-805
CODEN: MOMEF3; ISSN: 1076-1551
AU Gijbels, Koenraad; Brocke, Stefan; Abrams, John S.; Steinman, Lawrence
PY 1995
AB The authors previously demonstrated the local prodn. of the pleiotropic cytokine interleukin-6 (IL-6) in the central nervous system (CNS) in exptl. autoimmune encephalomyelitis (EAE), an animal model for the human disease multiple sclerosis. To assess the role of IL-6 in autoimmune CNS inflammation, the authors **administered** neutralizing antibodies to IL-6 in the EAE model. Their effect was examd. at the clin. and histopathol. level. Levels of **administered** antibody and IL-6 bioactivity were

followed in serum and cerebrospinal fluid (CSF). Systemically **administered** antibodies penetrated into the fluid CSF in animals in which EAE was induced. **Administration** of anti-IL-6 reduced the development of actively induced as well as adoptively transferred EAE and was assocd. with increased levels of IL-6 activity in the CSF and to a lesser extent in the serum. Anti-IL-6 was still effective when given 1 day before the onset of disease signs in adoptively transferred EAE. The **disease**-reducing effect of anti-**IL-6** was also reflected at the pathol. level by the absence of inflammatory infiltrates in the CNS. The study indicates that IL-6 plays an important role in autoimmune CNS inflammation. However, due to the complex nature of the in vivo interactions of **administered** antibodies, the **disease**-reducing effect of the anti-**IL-6** antibodies could be caused by neutralization of IL-6 activity or by enhancement of IL-6 activity via induction of higher IL-6 levels in the CNS.

L17 ANSWER 14 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1995:842658 CAPLUS
DN 123:225947
TI Use of anti-TNF antibodies as drugs in **treating** **diseases** involving elevated **interleukin-6** serum levels
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
IN Stenzel, Roswitha; Kaul, Martin; Daum, Lothar; Kempeni, Joachim; Raab, Christa; Schaefer, Sibylle

APPLICATION NO.	DATE
WO 95-EP291	19950127
DE 94-4409513	19940319
CA 95-2182723	19950127
AU 95-15201	19950127
CN 95-191517	19950127
JP 95-520363	19950127
BR 95-6741	19950127
EP 95-906353	19950127
HU 96-2169	19950127
ZA 95-956	19950207
FI 96-3101	19960806
NO 96-3280	19960806

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9520978	A1	19950810	WO 95-EP291	19950127

W: AU, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, MX, NO, NZ, PL, RU, SI, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

DE 4409513	C1	19951019	DE 94-4409513	19940319
CA 2182723	AA	19950810	CA 95-2182723	19950127
AU 9515201	A1	19950821	AU 95-15201	19950127
CN 1140414	A	19970115	CN 95-191517	19950127
JP 09509411	T2	19970922	JP 95-520363	19950127
BR 9506741	A	19971021	BR 95-6741	19950127
EP 804236	A1	19971105	EP 95-906353	19950127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI				
HU 76875	A2	19971229	HU 96-2169	19950127
ZA 9500956	A	19951011	ZA 95-956	19950207
FI 9603101	A	19960806	FI 96-3101	19960806
NO 9603280	A	19961004	NO 96-3280	19960806

PY 1995
1995
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1996

AB Tumor necrosis factor (TNF) antagonists, esp. anti-TNF antibodies and their fragments, are useful in prodn. of drugs to **treat diseases** characterized by elevated **interleukin-6** serum levels, e.g. sepsis.

L17 ANSWER 15 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1995:575935 CAPLUS
DN 122:306664
TI Rapid and sensitive enzyme-linked immunosorbent assay for measurement of HGF in rat and human tissues
SO Biomed. Res. (1995), 16(2), 105-14
CODEN: BRESD5; ISSN: 0388-6107
AU Yamada, Akira; Matsumoto, Kunio; Iwanari, Hiroko; Sekiguchi, Kiyoshi; Kawata, Sumio; Matsuzawa, Yuji; Nakamura, Toshikazu
PY 1995
AB Hepatocyte growth factor (HGF) has organotrophic functions for regeneration of the liver, kidney and lung, through mitogenic, and morphogenic activities. HGF concn. increases in sera of patients with various liver, kidney, and lung diseases. The authors designed a rapid and sensitive ELISA to measure HGF in crude tissue exts. **Monoclonal** antibodies to human HGF were prepd. and a **monoclonal** antibody (**mAb**) which cross-reacts with rat HGF was selected. Using the **mAb** as the first antibody and polyclonal antibody to rat or human HGF as the second antibody,

sandwich ELISA for the measurement of rat or human HGF was set up. This ELISA can specifically detect even 0.1 ng/mL rat or human HGF. Moreover, when endogenous biotin is blocked, HGF in tissue exts. can be measured directly and rapidly using this system. HGF level in livers of CCl4-**administered** rats was 5.5-fold higher than that in healthy livers 24 h after the **administration** and HGF level in kidneys of HgCl2-**administered** rats was 1.3-fold higher than that of the normal at 12 h after **administration**. Rapid measurement of HGF in tissues by this method should prove useful to elucidate mechanisms of tissue regeneration and the pathogenesis of various diseases.

L17 ANSWER 16 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1995:374865 CAPLUS
DN 122:158627
TI Reconstruction of chimeric mouse/human antibody against human interleukin-6
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
IN Tsuchiya, Masayuki; Sato, Koh; Hirata, Yuichi

APPLICATION NO.	DATE
WO 94-JP859	19940530
JP 94-115367	19940527
AU 94-68081	19940530
ZA 94-3778	19940530
US 96-553501	19960220

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9428159	A1	19941208	WO 94-JP859	19940530
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, KG, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 07046998	A2	19950221	JP 94-115367	19940527
AU 9468081	A1	19941220	AU 94-68081	19940530
ZA 9403778	A	19950221	ZA 94-3778	19940530
US 5856135	A	19990105	US 96-553501	19960220

PY 1994
1995
1994
1995
1999

AB Disclosed is a reconstructed anti-human IL-6 antibody. The L chain of the chimeric antibody is comprised of the C and FR regions of human origin as well as the CDR regions of anti-human IL-6 **monoclonal** antibody (**MAb**; e.g. SK2) of mouse. The H chain of the chimeric antibody is comprised of the C and FR

regions of human origin as well as the CDR regions of anti-human IL-6 **MAb** of mouse. This reconstructed antibody has a low antigenicity against humans because its major components are originated in a human antibody and the mouse CDR has a low antigenicity. The humanized antibody can be used for the **treatment** of **diseases** caused by **IL-6**. Prepn. of plasmids such as HEF-SK2h-NTS and their expression in COS cells were demonstrated.

L17 ANSWER 17 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1995:235931 CAPLUS
DN 122:7638
TI Inhibition of interleukin 2 production and alteration of interleukin 2 mRNA processing by human T-T cell hybridoma-derived suppressor factors
SO Hybridoma (1994), 13(5), 343-52
CODEN: HYBRDY; ISSN: 0272-457X
AU Fox, Floyd E.; Chernajovsky, Yuti; Platsoucas, Chris D.
PY 1994
AB Investigated were the mechanisms by which two human T-T cell hybridoma-derived suppressor factors (SFs) (designated 160 and 169) (Platsoucas et al., Hybridoma 1987;6:589; Kunicka et al., Hybridoma 1989;8:127) inhibit the proliferative response to mitogens by human peripheral blood mononuclear cells (PBMCs). Interleukin 2 (IL-2) prodn. by human PBMCs cultured with Con A or OKT3 **monoclonal** antibody for 12 or 36 h in the presence of 160 or 169 SF was found to be inhibited >80% when compared to control PBMC cultures stimulated with mitogen in the absence of SFs. This suppression of IL-2 prodn. was not due to the SFs interfering with IL-2-induced proliferation of the IL-2-dependent murine cell clone used to det. the levels of IL-2. The proliferative responses of SF-treated PBMCs could not be restored by addn. of exogenous recombinant human IL-2 (rIL-2) (1-100 U/mL). Furthermore, inhibition of the proliferative responses by the SFs could not be reversed by addn. of exogenous rIL-1, rIL-2, or rIL-4 alone or in paired combinations. The expression of IL-2 receptors (TAC Ag) on Con A-activated cultures at 12- or 36-h time points was not affected by treatment with the SFs. Both the 160 and 169 hybridoma-derived SFs were found to cause the accumulation of an mRNA of 2.8 kb that hybridized with an IL-2-specific oligonucleotide probe. This 2.8-kb transcript was in addn. to the expected 1.0-kb, transiently expressed IL-2 message, and it could be superinduced in the presence of cycloheximide. These results suggest that these SFs may be influencing RNA splicing pathways. These SFs appear to be useful mols. for probing the regulatory controls of lymphocyte proliferation and may constitute important physiol. regulators of the immune response. In addn., they may have clin. activity for the treatment of patients that received transplants, patients with autoimmune diseases, and others.

L17 ANSWER 18 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1994:678320 CAPLUS
DN 121:278320
TI Effects of anti-interferon-.gamma. and anti-**interleukin-6** antibodies in **disease** models in mice: antibodies as carriers of cytokines
SO J. Interferon Res. (1994), 14(5), 277-9
CODEN: JIREDJ; ISSN: 0197-8357
AU Billiau, A.; Matthys, P.; Martens, E.; Heremans, H.
PY 1994
AB A review with 7 refs. The **administration** of neutralizing antibodies to interleukin-6 or interferon-.gamma. results in a paradoxical increase in serum cytokine titers. While protective in endotoxin shock models, the results raise 2 questions: (1) what are the underlying mechanisms and (2) how are increased levels related to protection against manifestations of disease. For interleukin-6, **monoclonal** antibodies **administered** to animals or human patients serve a dual role. On one hand, they withhold any interleukin-6 that is released in to the circulation from interacting with receptors on cells; on the other hand, they also prevent elimination of the cytokine from circulation. This situation can be considered to apply to any cytokine. However, crit. conditions required for circulating antibody to act as a carrier rather than as a neutralizer are that the antibody becomes almost completely sat. with cytokine and that the equimolar mixt. is biol. active.

L17 ANSWER 19 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1994:603363 CAPLUS
DN 121:203363
TI Progenitor B cell stimulating factor
SO Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
IN Samal, Babru Bahan

	APPLICATION NO.	DATE
AI	EP 93-118600	19931118
	WO 93-US11242	19931118
	CA 93-2149763	19931118
	AU 94-56135	19931118
	CN 93-121435	19931118
	JP 93-513260	19931118
	AT 93-118600	19931118
	ES 93-118600	19931118
	US 94-294770	19940823

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 601360	A1	19940615	EP 93-118600	19931118
	EP 601360	B1	19971022		

	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	WO 9412535	A1	19940609	WO 93-US11242	19931118
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2149763	AA	19940609	CA 93-2149763	19931118
	AU 9456135	A1	19940622	AU 94-56135	19931118
	AU 680851	B2	19970814		
	CN 1094093	A	19941026	CN 93-121435	19931118
	JP 08505373	T2	19960611	JP 93-513260	19931118
	AT 159545	E	19971115	AT 93-118600	19931118
	ES 2108189	T3	19971216	ES 93-118600	19931118
	US 5580754	A	19961203	US 94-294770	19940823
PY	1994				
	1997				
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AB A progenitor B cell stimulating factor (PBSF) which promotes the formation of pre-B cells is described. DNA sequences encoding same and methods of prodn. and purifn. of the factor are also disclosed. The factor is used in the treatment of hematopoietic disorders and in bone marrow transplantation.

L17 ANSWER 20 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1994:407322 CAPLUS
DN 121:7322
TI Interleukin-6 analogs as antagonists of the receptor
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
IN Brakenhoff, Just Pj.; Aarden, Lucien A.

	APPLICATION NO.	DATE
AI	WO 93-US10051	19931020
	CA 93-2147466	19931020
	AU 94-54092	19931020
	EP 93-924383	19931020
	JP 93-510369	19931020
	US 94-357538	19941216
	US 95-476651	19950607

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9409138	A1	19940428	WO 93-US10051	19931020
	W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2147466	AA	19940428	CA 93-2147466	19931020
	AU 9454092	A1	19940509	AU 94-54092	19931020
	AU 687763	B2	19980305		
	EP 672144	A1	19950920	EP 93-924383	19931020
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09505721	T2	19970610	JP 93-510369	19931020
	US 5591827	A	19970107	US 94-357538	19941216
	US 5723120	A	19980303	US 95-476651	19950607
PY	1994				
	1994				
	1994				
	1998				
	1995				
	1997				
	1997				
	1998				

AB A class of interleukin-6 (IL-6) analogs that act as IL-6 receptor antagonists and that inhibit the normal function of naturally-occurring IL-6 are described. These IL-6 receptor antagonists are preferably IL-6 mols. contg. one or more mutations in the Site II (amino acids 145-163). These antagonists can be used in pharmaceuticals for **treating IL-6** related **diseases** such as sepsis and multiple myeloma. Mutants were prepd. by random mutagenesis of the region encoding Gln-153-Thr-163 and screened for retention of binding to a site I-specific **monoclonal** antibody and loss of binding to a site-II specific **monoclonal** antibody. The resulting mutants were then assayed for growth factor activity in the B9 assay and for B-cell stimulatory factor-2 activity in the CESS assay. All the analogs were active in the B9 assay but two (Thr-163.fwdarw.Pro and Ala-154.fwdarw.Glu, Gln-160.fwdarw.His) were inactive in the CESS assay. These two analogs were manufd. in Escherichia coli as inclusion bodies, solubilized and purified and tested for their ability to antagonize IL-6 activity. The analogs antagonized IL-6 activity in a no. of cell lines with the antagonism reversible by high levels of IL-6, suggesting that inhibition was by competitive inhibition.

L17 ANSWER 21 OF 29 CAPLUS
AN 1994:321368 CAPLUS

DN 120:321368
TI **Monoclonal** antibodies to interleukin 6 receptor (IL-6R), and their diagnostic and medical applications
SO Fr. Demande, 20 pp.
CODEN: FRXXBL
IN Wijdenes, John; Clement, Claude; Marchand, Delphine

APPLICATION NO.	DATE
FR 92-10005	19920813

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2694767	A1	19940218	FR 92-10005	19920813
FR 2694767	B1	19941021		

PY 1994
1994
AB **Monoclonal** antibodies (**MAbs**) to IL-6R for human IL-6 are presented. The **MAbs** are useful for medicaments to **treat**, e.g., multiple myeloma, Castleman's **disease**, and other **IL-6**-dependent maladies. The **MAbs** are also useful for the detection of IL-6R or an epitope thereof. **MAbs** B-F19, B-R6, and B-N12 were prepd. by the hybridoma method, purified, and characterized. The 3 **MAbs** recognize different epitopes of IL-6R. Sol. IL-6R was detd. by sandwich ELISA using 2 of the **MAbs**.

L17 ANSWER 22 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1994:161201 CAPLUS
DN 120:161201
TI Mechanisms of paraneoplastic syndromes of colon-26: involvement of interleukin 6 in hypercalcemia
SO Cytokine (Philadelphia) (1993), 5(5), 463-8
CODEN: CYTIE9; ISSN: 1043-4666
AU Strassmann, Gideon; Jacob, Chaim O.; Fong, Miranda; Bertolini, Donald R.
PY 1993
AB The precise mechanisms responsible for increased calcium levels in patients with cancer are not fully understood. In a recent study, the participation of interleukin (IL)-6 as an important mediator of key parameters of cancer cachexia in the colon-26 adenocarcinoma was reported. Here, the authors show that in addn. to cachexia, C-26 tumor bearing mice also develop hypercalcemia. Treatment of these mice with 5' deoxyfluorouridine reduced tumor size and inhibited both hypercalcemia, cachexia, and elevated serum IL-6. Moreover, **monoclonal** antibody to mouse IL-6 prevents both the cachexia and the hypercalcemia and reduces serum IL-6 levels in C-26 tumor bearing hosts. The **administration** of a bisphosphonate compd. (Clodronate) reverses the hypercalcemia but has no effect on tumor burden, serum IL-6 levels, or wasting. The authors conclude that tumor-derived IL-6 plays a role in the pathogenesis of the C-26

assocd. hypercalcemia, and that the increase of serum calcium does not by itself mediate cachexia.

L17 ANSWER 23 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1994:131813 CAPLUS
DN 120:131813
TI A **monoclonal** anti-human IL-6 receptor antibody inhibits the proliferation of human myeloma cells
SO Hybridoma (1993), 12(5), 621-30
CODEN: HYBRDY; ISSN: 0272-457X
AU Huang, Yi Wu; Vitetta, Ellen S.
PY 1993
AB A **monoclonal** antibody (UV4) against the human IL-6 receptor (hIL-6R) was generated by immunizing BALB/c mice with both a human myeloma cell line (U266) and a murine cell line (M12.4/R) transfected with the hIL-6R cDNA. Flow cytometric anal. demonstrated that UV4 stains the hIL-6R+ cell lines U266 and U937, but not the hIL-6R- cell lines Daudi and K562. Competitive inhibition assays demonstrated that preincubation of U266 cells with UV4 inhibited the binding of a phycoerythrin (PE)-IL-6 conjugate to the hIL-6R and also inhibited the proliferative activity of IL-6 on the IL-6-dependent human myeloma cell lines ILKM2 and ILKM3. In contrast, UV4 did not interfere with the proliferation of the hIL-6R- Burkitt's lymphoma cell line, Daudi. Direct sandwich RIAs further confirmed that the UV4 bound to the same mol. as the goat anti-hIL-6R antibody. These results suggest that both UV4 and human IL-6 bind to the same or adjacent epitopes on the hIL-6R. This **monoclonal** antibody should facilitate studies of the structure-function relationship of IL-6R and may be useful for the **treatment** of **IL-6**-dependent **diseases** such as multiple myeloma.

L17 ANSWER 24 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1994:69600 CAPLUS
DN 120:69600
TI A method for using lipoprotein-associated coagulation inhibitor (LACI) to treat inflammation, including sepsis or septic shock
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
IN Creasey, Abla A.

	APPLICATION NO.	DATE
AI	WO 93-US3860	19930423
	JP 93-500530	19930423

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9324143	A1	19931209	WO 93-US3860	19930423

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,

SE
JP 07507300 T2 19950810 JP 93-500530 19930423
PY 1993
1995
AB A method for prophylactically or therapeutically treating inflammation, including sepsis or septic shock, comprises **administration** of a therapeutically effective amt. of LACI. Inhibition of sepsis by LACI was tested in human umbilical vein endothelial cells using LPS as an inducer of sepsis, as well as in baboons receiving an i.v. Escherichia coli infusion.

L17 ANSWER 25 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1993:75727 CAPLUS
DN 118:75727
TI Hepatocyte nuclear factor 4 (HNF-4) and cloning of its cDNA
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
IN Sladek, Frances M.; Zhong, Weimin; Darnell, James E., Jr.

APPLICATION NO.	DATE
WO 91-US9733	19911223
CA 91-2098838	19911223
AU 91-91742	19911223
EP 92-903912	19911223
US 93-78222	19931028
US 96-661330	19960614

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9211365	A1	19920709	WO 91-US9733	19911223
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2098838	AA	19920622	CA 91-2098838	19911223
AU 9191742	A1	19920722	AU 91-91742	19911223
AU 665939	B2	19960125		
EP 564592	A1	19931013	EP 92-903912	19911223
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
US 5604115	A	19970218	US 93-78222	19931028
US 5849485	A	19981215	US 96-661330	19960614

PY 1992
1992
1992
1996
1993
1997
1998
AB DNA encoding HNF-4, cells producing HNF-4, methods of inhibiting HNF-4 function, and treatment of diseases by **administering** ligands for HNF-4 or apoCIII are claimed. The cDNA for rat liver HNF-4 was cloned and sequenced. HNF-4 has a structure analogous to

the steroid/thyroid hormones receptors: it contains a zinc finger domain, and a hydrophobic C-terminus with similarity to the ligand binding domain of the other receptors. Also in the C-terminus is a proline-rich region characteristic of activator domains and possible phosphorylation sites. HNF-4 binds to its recognition site as a dimer. HNF-4 mRNA is present in liver, kidney, and intestine, but not in spleen, brain, white fat, lung, or heart. The factor binds to LF-A1 sites, but does not bind significantly to ERE, TRE, or GRE sites.

L17 ANSWER 26 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1993:57915 CAPLUS
DN 118:57915
TI Interleukin-6 in mouse hypersensitivity pneumonitis: changes in lung free cells following depletion of endogenous IL-6 or direct **administration** of IL-6
SO J. Leukocyte Biol. (1992), 52(2), 197-201
CODEN: JLBIE7; ISSN: 0741-5400
AU Denis, Michel
PY 1992
AB This study examd. the role of interleukin-6 (IL-6) in the development of chronic lung inflammatory conditions, using a mouse model of hypersensitivity pneumonitis established by intranasal instillation of the thermophilic actinomycete Faeni rectivirgula. Challenged mice developed an early neutrophilic response at 24 h, followed by a macrophage/lymphocyte recruitment. The impact of IL-6 on the development of the inflammatory response was assessed by giving infusions of a **monoclonal** antibody against IL-6 so as to deplete endogenous levels of this cytokine or by giving exogenous IL-6 to challenged mice. Mice challenged intranasally with the actinomycete and given the anti-IL-6 antibody developed a strong, sustained neutrophilic response, with a higher lung free cell no. than control mice. Assessment of fibrosis by measuring lung hydroxyproline levels showed that challenged mice given anti-IL-6 developed more significant fibrosis than control mice. Conversely, infusions with IL-6 diminished F. rectivirgula-induced cell recruitments and the fibrotic response in the lungs. Moreover, alveolar macrophages from mice given 2 wk of F. rectivirgula treatment released high levels of tumor necrosis factor .alpha. (TNF-.alpha.) bioactivity upon in vitro lipopolysaccharide challenge, compared to mice instilled with saline only. This TNF-.alpha. activity produced by macrophages was decreased by in vivo IL-6 treatment and enhanced by in vivo neutralization with anti-IL-6. Apparently, IL-6 may play a role in regulating the cellular recruitment in the lungs during an inflammatory response, with dramatic consequences for the cellular profile in the bronchoalveolar lavage and the subsequent fibrosis.

L17 ANSWER 27 OF 29 CAPLUS COPYRIGHT 1999 ACS

AN 1993:37393 CAPLUS
DN 118:37393
TI Tumor necrosis factor and interleukin-6 in Candida albicans infection in normal and granulocytopenic mice
SO Infect. Immun. (1992), 60(10), 4003-8
CODEN: INFIBR; ISSN: 0019-9567
AU Steinshamn, Sigurd; Waage, Anders
PY 1992
AB The authors **administered** a neutralizing **monoclonal** antibody to tumor necrosis factor (TNF) during infection with C. albicans in normal and granulocytopenic mice. Mice were rendered granulocytopenic (<0.1 .times. 109 granulocytes per L) with cyclophosphamide. Growth of C. albicans from the kidneys was increased in normal mice treated with the antibody to TNF, compared with that in control mice, after 36 h (3.6 .times. 104 CFU per kidney vs. 9.1 .times. 103 CFU per kidney) and after 72 h (3.7 .times. 106 CFU per kidney vs. 2.3 .times. 104 CFU per kidney). In granulocytopenic mice, the antibody to TNF had no effect on the growth of C. albicans from the kidneys. Furthermore, the cytokines TNF and interleukin-6 (IL-6) were produced in a dose-dependent manner during C. albicans infection. TNF was detectable between 6 and 60 h, with peak levels at 24 h. Both TNF and IL-6 levels were higher in cyclophosphamide-treated mice than in normal mice. Heat-inactivated C. albicans induced a TNF response different from that induced by viable C. albicans, with an early peak occurring at 3 to 4 h and declining to nondetectable levels after 15 to 24 h. Peak levels of TNF obtained with heat-inactivated C. albicans were lower than those obtained with viable C. albicans. Thus, TNF and IL-6 are produced systemically during C. albicans infection and TNF is essential for granulocyte antifungal activity in vivo.

L17 ANSWER 28 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1992:563879 CAPLUS
DN 117:163879
TI Anti-interleukin-6 receptor antibody as interleukin-6 inhibitor
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
IN Kishimoto, Chuzo; Suzuki, Hiroshi; Yasukawa, Kyoshi

APPLICATION NO.	DATE
JP 90-315792	19901122

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04187645	A2	19920706	JP 90-315792	19901122

PY 1992
AB Anti-interleukin-6 receptor antibody inhibits interleukin-6 action, esp. interleukin-6-related blood platelet increase and, thus, may be used in clin. therapy. Anti-interleukin-6 receptor **monoclonal** antibody enhanced anti-interleukin-6 antibody

prodn. in mice.

L17 ANSWER 29 OF 29 CAPLUS COPYRIGHT 1999 ACS
AN 1992:188667 CAPLUS
DN 116:188667
TI Hepatocyte growth factor as therapeutic and diagnostic agent for renal diseases and as growth-promoting agent for cultured nephrocytes
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
IN Nakamura, Toshikazu

	APPLICATION NO.	DATE
AI	EP 91-109923	19910618
	JP 90-158841	19900619

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 462549	A1	19911227	EP 91-109923	19910618
	EP 462549	B1	19960828		
	R: CH, DE, FR, GB, IT, LI				
	JP 04049246	A2	19920218	JP 90-158841	19900619
	JP 2750372	B2	19980513		

PY 1991
1996
1992
1998

AB Hepatocyte growth factor (HGF) is an active ingredient in therapeutic and preventive agents for renal diseases, in a diagnostic agent for renal diseases, and in an agent for growth of cultured nephrocytes. The therapeutic and preventive agent promotes regeneration of nephrocytes in chronic nephritis and prevents transition to renal failure, while promoting regeneration of the kidney with renal failure and recovering renal functions to a normal state. The diagnostic for renal diseases can detect or det. HGF in tissues or blood. The nephrocyte growth-promoting agent has specificity and growth-promoting activity in the in vitro nephrocyte cultivation system. Isolation of HGF from rat liver and recombinant prodn. of HGF are described. Soln. and injection compns. are presented. Rat HGF showed dose-dependent growth-promoting activity for rat kidney proximal tubular cells.

=> d his l18-; d 1-33 .bevpat

(FILE 'USPATFULL' ENTERED AT 14:53:33 ON 15 JAN 1999)
L18 34 S L15
L19 33 S L18 NOT L5

L19 ANSWER 1 OF 33 USPATFULL
Searcher : Shears 308-4994

AN 1999:4038 USPATFULL
TI Methods for the treatment of wounds using butyric acid salts and derivatives
IN Faller, Douglas V, Braintree, MA, United States
PA Trustees of Boston University, Boston, MA, United States (U.S. corporation)
PI US 5858365 990112
AI US 95-473957 950607 (8)
RLI Division of Ser. No. US 93-142908, filed on 29 Oct 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Minnifield, Nita
LREP Kenyon & Kenyon
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 41 Drawing Figure(s); 21 Drawing Page(s)
LN.CNT 1870
AB This invention is directed to methods of administering physiologically stable and safe compositions of butyric acid salts and derivatives to a patient for the purpose of wound healing.

INCL INCLM: 424/184.100
INCLS: 424/278.100; 536/115.000; 536/119.000; 514/012.000; 514/551.000; 514/925.000; 514/926.000; 514/927.000; 514/928.000
NCL NCLM: 424/184.100
NCLS: 424/278.100; 536/115.000; 536/119.000; 514/012.000; 514/551.000; 514/925.000; 514/926.000; 514/927.000; 514/928.000

L19 ANSWER 2 OF 33 USPATFULL
AN 1998:159986 USPATFULL
TI Phenylacetate and derivatives alone or in combination with other compounds against neoplastic conditions and other disorders
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5852056 981222
WO 9510271 950420
AI US 96-633833 960410 (8)
WO 94-US11492 941012
960410 PCT 371 date
960410 PCT 102(e) date
RLI Continuation of Ser. No. US 94-207521, filed on 7 Mar 1994, now patented, Pat. No. US 5605930 And Ser. No. US 93-135661, filed on 12 Oct 1993, now patented, Pat. No. US 5635532 , each Ser. No. US - which is a continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991, now abandoned

DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 32 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 5051
AB Methods of inhibiting IL-6 in a cell by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof.

INCL INCLM: 514/510.000
INCLS: 514/513.000; 514/515.000; 514/529.000; 514/538.000; 514/563.000; 514/567.000
NCL NCLM: 514/510.000
NCLS: 514/513.000; 514/515.000; 514/529.000; 514/538.000; 514/563.000; 514/567.000

L19 ANSWER 3 OF 33 USPATFULL
AN 1998:159755 USPATFULL
TI Inflammation-induced expression of a recombinant gene
IN Munford, Robert S., Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5851822 981222
AI US 98-67908 980428
RLI Division of Ser. No. US 95-456103, filed on 30 May 1995, now patented, Pat. No. US 5744304
DT Utility
EXNAM Primary Examiner: Ketter, James
LREP Arnold, White & Durkee
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1664
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes methods of controlling and regulating the inflammatory reaction generated in response to various toxins, immunogens, pathogens and autoimmune insults. The method employs a vector that includes an anti-cytokine protein or antibacterial protein gene under the control of a cytokine responsive promoter. In animal models, adenoviral vectors successfully delivered the vectors to hepatic cells and were subsequently shown to respond only to stimulation by induced cytokines.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/320.100
INCLS: 435/235.100; 536/023.500

NCL NCLM: 435/320.100
NCLS: 435/235.100; 536/023.500

L19 ANSWER 4 OF 33 USPATFULL
AN 1998:156907 USPATFULL
TI Human interleukin-6 receptor antagonists
IN Ciliberto, Gennaro, Rome, Italy
Savino, Rocco, Rome, Italy
Lahm, Armin, Rome, Italy
Toniatti, Carlo, Rome, Italy
PA Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A., Rome, Italy (non-U.S. corporation)
PI US 5849283 981215
WO 9618648 960620
AI US 96-693182 960814 (8)
WO 95-IT216 951213
960814 PCT 371 date
960814 PCT 102(e) date
PRAI IT 94-M805 941214
DT Utility
EXNAM Primary Examiner: Ulm, John; Assistant Examiner: Mertz, Prema
LREP Browdy and Neimark
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 439
AB It is known that the ligands of the group of cytokines similar to Interleukin 6 (IL-6), that is Oncostatin M (OSM), Leukemia Inhibitory Factor (LIF), Ciliary Neurotrophic Factor (CNTF) and Interleukin 11 (IL-11), induce the formation of a receptor complex of which the membrane molecule gp 130 is a part. The present invention refers to a methodology for selecting superagonists, antagonists and superantagonists of human interleukin-6 comprising the following operations: comparing the amino acid sequence of bovine granulocyte colony stimulating factor (bG-CSF) with the sequence of said hormone; and on the basis of the above comparison, formulating a three dimensional model of said hormone, which allows the identification of residues that form the site of interaction with the specific receptor (Site 1) and those that constitute the site of interaction with gp 130 (Site 2) respectively. The invention allows the identification of these sites in human interleukin-6 and the isolation of variants having, with respect to the wild type hormone, a greater affinity for the specific receptor (superagonists and superantagonists) or affinity for gp 130 reduced or abolished (antagonists and superantagonists). The figure shows a scheme illustrating the methodology applied to identify site 1 and site 2 in the case of human interleukin-6. The invention also describes the obtaining of specific superagonists and superantagonists of interleukin-6 and

the use of superantagonists as low dose inhibitors of the growth of human myeloma cells dependent on wild type interleukin-6. (FIG. 1)

INCL INCLM: 424/085.200
INCLS: 530/351.000; 514/002.000; 514/008.000; 514/012.000; 930/141.000; 435/252.300; 435/252.330; 435/320.100; 435/069.520; 435/071.100; 435/071.200; 435/172.100; 435/172.300
NCL NCLM: 424/085.200
NCLS: 435/069.520; 435/071.100; 435/071.200; 435/252.300; 435/252.330; 435/320.100; 514/002.000; 514/008.000; 514/012.000; 530/351.000; 930/141.000

L19 ANSWER 5 OF 33 USPATFULL
AN 1998:154080 USPATFULL
TI DNA encoding tumor necrosis factor stimulated gene 6 (TSG-6)
IN Lee, Tae Ho, Daejeon, Korea, Republic of
Wisniewski, Hans-Georg, New York, NY, United States
Vilcek, Jan, New York, NY, United States
PA New York University, New York, NY, United States (U.S. corporation)
PI US 5846763 981208
AI US 94-242097 940513 (8)
RLI Continuation-in-part of Ser. No. US 93-24868, filed on 1 Mar 1993, now patented, Pat. No. US 5386013 which is a continuation of Ser. No. US 91-642312, filed on 14 Jan 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Draper, Garnette D.; Assistant Examiner: Kemmerer, Elizabeth C.
LREP Browdy and Neimark
CLMN Number of Claims: 14
ECL Exemplary Claim: 2
DRWN 48 Drawing Figure(s); 28 Drawing Page(s)
LN.CNT 3798
AB TSG-6 protein and functional derivatives thereof, DNA coding therefor, expression vehicles, such as a plasmids, and host cells transformed or transfected with the DNA molecule, and methods for producing the protein and the DNA are provided, as well as antibodies specific for the TSG-6 protein; a method for detecting the presence of TSG-6 protein in a biological sample; a method for detecting the presence of nucleic acid encoding a normal or mutant TSG-6 protein; a method for measuring induction of expression of TSG-6 in a cell using either nucleic acid hybridization or immunoassay; a method for identifying a compound capable of inducing the expression of TSG-6 in a cell; and a method for measuring the ability of a cell to respond to TNF.

INCL INCLM: 435/069.100

INCLS: 435/320.100; 435/172.300; 435/252.300; 536/023.500; 536/023.100
NCL NCLM: 435/069.100
NCLS: 435/252.300; 435/320.100; 536/023.100; 536/023.500

L19 ANSWER 6 OF 33 USPATFULL
AN 1998:151097 USPATFULL
TI Cytokine antagonists
IN Stahl, Neil, Carmel, NY, United States
Economides, Aris, Dobbs Ferry, NY, United States
Yancopoulos, George D., Yorktown Heights, NY, United States
PA Regeneron Pharmaceuticals, Inc., Tarrytown, NY, United States (U.S. corporation)
PI US 5844099 981201
AI US 95-563105 951127 (8)
RLI Continuation-in-part of Ser. No. US 93-140222, filed on 20 Oct 1993, now patented, Pat. No. US 5470952
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Hayes, Robert C.
LREP Kempler, Gail
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 24 Drawing Figure(s); 21 Drawing Page(s)
LN.CNT 1651
AB Heteromeric proteins comprising a soluble .alpha. specificity determining cytokine receptor component and the extracellular domain of a .beta. receptor component function as cytokine antagonists.

INCL INCLM: 530/350.000
INCLS: 530/351.000; 530/402.000; 530/399.000; 424/085.200
NCL NCLM: 530/350.000
NCLS: 424/085.200; 530/351.000; 530/399.000; 530/402.000

L19 ANSWER 7 OF 33 USPATFULL
AN 1998:150994 USPATFULL
TI Compositions and methods for treating and preventing pathologies including cancer
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represeneted by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5843994 981201
AI US 95-478264 950607 (8)
RLI Division of Ser. No. US 94-207521, filed on 7 Mar 1994, now patented, Pat. No. US 5605930 which is a continuation-in-part of Ser. No. US 93-135661, filed on 12 Oct 1993, now abandoned which is a continuation-in-part of Ser. No. US 91-779744, filed on 21

Oct 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle&Rosenberg, P.C.
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN 63 Drawing Figure(s); 43 Drawing Page(s)
LN.CNT 7935
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents including retinoids, hydroxyurea, and flavonoids. Intravesicle methods of treatment of cancers phenylacetate. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention. A product as a combined preparation of phenylacetate and a retinoid, hydroxyurea, or flavonid (or other mevalonate pathway inhibitor) for simultaneous, separate, or sequential use in treating a neoplastic condition in a subject. Methods of modulating lipid metabolism and/or reducing serum triglycerides in a subject using phenylacetate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/510.000
INCLS: 514/513.000; 514/515.000; 514/529.000; 514/538.000; 514/563.000; 514/567.000
NCL NCLM: 514/510.000
NCLS: 514/513.000; 514/515.000; 514/529.000; 514/538.000; 514/563.000; 514/567.000

L19 ANSWER 8 OF 33 USPATFULL
AN 1998:92168 USPATFULL
TI Interleukin-6 receptor antagonists
IN Savino, Rocco, Pomezia, Italy
Lahm, Armin, Rome, Italy
Cillberto, Gennaro, Casalpalocco, Italy
PA Istituto di Ricerche di Biologica Molecolare P. Angeletti S.p.A., Pomezia, Italy (non-U.S. corporation)
PI US 5789552 980804
AI US 95-567047 951204 (8)
RLI Division of Ser. No. US 95-387924, filed on 23 Feb 1995
PRAI IT 93-RM409 930623
DT Utility
EXNAM Primary Examiner: Ulm, John; Assistant Examiner: Saoud, Christine
LREP Browdy and Neimark

CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 909
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are interleukin-6 receptor antagonists. These receptor antagonists are generated by mutating amino acid positions 31, 35, 118, 121, 175, 176 and/or 183 of human interleukin-6.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/351.000
INCLS: 435/069.520; 435/325.000; 435/252.300; 435/320.100; 930/140.000
NCL NCLM: 530/351.000
NCLS: 435/069.520; 435/252.300; 435/320.100; 435/325.000; 930/140.000

L19 ANSWER 9 OF 33 USPATFULL
AN 1998:86040 USPATFULL
TI Receptor for oncostatin M
IN Mosley, Bruce, Seattle, WA, United States
Cosman, David J., Bainbridge Island, WA, United States
PA Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI US 5783672 980721
AI US 94-308881 940912 (8)
RLI Continuation-in-part of Ser. No. US 94-249553, filed on 26 May 1994, now abandoned
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Gucker, Stephen
LREP Anderson, Kathryn A.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2127
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel polypeptide functions as the .beta. chain of an oncostatin M receptor and is thus designated OSM-R.beta.. Heterodimeric receptor proteins comprising OSM-R.beta. and gp130 bind oncostatin M and find use in inhibiting biological activities mediated by oncostatin M.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/350.000
INCLS: 530/395.000; 530/402.000
NCL NCLM: 530/350.000
NCLS: 530/395.000; 530/402.000

L19 ANSWER 10 OF 33 USPATFULL

AN 1998:82887 USPATFULL
TI Oligonucleotides specific for cytokine signal transducer gp130 mRNA
IN Becherer, Kathleen Ann, San Diego, CA, United States
Dattagupta, Nanibhushan, San Diego, CA, United States
Naidu, Yathi M., Park Ridge, IL, United States
PA Gen-Probe Incorporated, San Diego, CA, United States (U.S. corporation)
PI US 5780612 980714
AI US 97-943834 971003 (8)
RLI Continuation of Ser. No. US 95-476634, filed on 7 Jun 1995, now patented, Pat. No. US 5674995
DT Utility
EXNAM Primary Examiner: LeGuyader, John L.; Assistant Examiner: McGarry, Sean
LREP Cappellari, Charles B.; Fisher, Carlos A.
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 817
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to oligonucleotides which are effective inhibitors of disease-associated cellular proliferation. In particular, it relates to the use of oligonulceotides which are substantially complementary to gp130 mRNA sequences. In the form of pharmaceutical compositions, these oligonucleotides are suitable for administration to human subjects for the treatment of abnormal cellular proliferation due to such diseases as cancer, autoimmune disorders and viral infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 536/024.500
INCLS: 435/006.000; 435/172.100; 536/023.100; 536/024.300; 536/024.100
NCL NCLM: 536/024.500
NCLS: 435/006.000; 536/023.100; 536/024.100; 536/024.300

L19 ANSWER 11 OF 33 USPATFULL
AN 1998:48388 USPATFULL
TI Method for inhibiting cellular proliferation using antisense oligonucleotides to gp130 mRNA
IN Becherer, Kathleen, San Diego, CA, United States
Dattagupta, Nanibhushan, San Diego, CA, United States
Naidu, Yathi M., Park Ridge, IL, United States
PA Gen-Probe Incorporated, San Diego, CA, United States (U.S. corporation)
PI US 5747470 980505
AI US 95-484518 950607 (8)
DT Utility

EXNAM Primary Examiner: Ketter, James; Assistant Examiner: Yucel, Irem
LREP Cappellari, Charles B.; Fisher, Carlos A.
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 875
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods of treating disease-associated cellular proliferation using oligonucleotides. In particular, it relates to the use of oligonulceotides which are substantially complementary to gp130 mRNA sequences. In the form of pharmaceutical compositions, these oligonucleotides are suitable for administration to human subjects for the treatment of abnormal cellular proliferation due to such diseases as cancer, autoimmune disorders and viral infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/044.000
INCLS: 424/450.000; 536/024.310; 536/024.330; 536/024.500
NCL NCLM: 514/044.000
NCLS: 424/450.000; 536/024.310; 536/024.330; 536/024.500

L19 ANSWER 12 OF 33 USPATFULL
AN 1998:45047 USPATFULL
TI Inflammation-induced expression of a recombinant gene
IN Munford, Robert S., Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5744304 980428
AI US 95-456103 950530 (8)
DT Utility
EXNAM Primary Examiner: Ketter, James
LREP Arnold, White & Durkee
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1661
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes methods of controlling and regulating the inflammatory reaction generated in response to various toxins, immunogens, pathogens and autoimmune insults. The method employs a vector that includes an anti-cytokine protein or antibacterial protein gene under the control of a cytokine responsive promoter. In animal models, adenoviral vectors successfully delivered the vectors to hepatic cells and were subsequently shown to respond only to stimulation by induced cytokines.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/006.000
INCLS: 435/172.300; 435/069.100; 514/044.000
NCL NCLM: 435/006.000
NCLS: 435/069.100; 514/044.000

L19 ANSWER 13 OF 33 USPATFULL
AN 1998:21887 USPATFULL
TI Method of **treating** an **IL-6** related **disease** with **interleukin-6** receptor antagonists
IN Brakenhoff, Just P. J., Amsterdam, Netherlands
Aarden, Lucien A., Broek In Waterland, Netherlands
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, Netherlands (non-U.S. corporation)
PI US 5723120 980303
AI US 95-476651 950607 (8)
RLI Division of Ser. No. US 94-357538, filed on 16 Dec 1994, now patented, Pat. No. US 5591827 which is a continuation of Ser. No. US 92-959942, filed on 20 Oct 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Ulm, John; Assistant Examiner: Mertz, Prema
LREP Rin-Laures, Li-Hsien; Savereide, Paul B.; Blackburn, Robert P.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1364
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a class of interleukin-6 (IL-6) muteins which act as IL-6 receptor antagonists, thereby inhibiting the normal function of naturally-occurring IL-6. These IL-6 receptor antagonism are preferably IL-6 molecules containing one or more mutations in the Site II region comprising amino acids 154-163. This invention also provides pharmaceutical compositions comprising IL-6 receptor antagonists with a pharmaceutically acceptable carrier. This invention further provides methods for **treating IL-6** related **diseases** such as sepsis and multiple myeloma, the methods comprising administering to a patient an IL-6 receptor antagonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.200
INCLS: 514/002.000; 514/012.000; 514/885.000; 530/351.000
NCL NCLM: 424/085.200
NCLS: 514/002.000; 514/012.000; 514/885.000; 530/351.000

L19 ANSWER 14 OF 33 USPATFULL
AN 1998:9533 USPATFULL

TI Methods of inducing the production of hemoglobin and treating pathologies associated with abnormal hemoglobin activity using phemylacetic acids and derivatives therof
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5712307 980127
AI US 95-465924 950606 (8)
RLI Division of Ser. No. US 93-135661, filed on 12 Oct 1993 which is a continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg,P.C.
CLMN Number of Claims: 40
ECL Exemplary Claim: 1
DRWN 32 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 4169
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/538.000
INCLS: 514/563.000; 514/567.000
NCL NCLM: 514/538.000
NCLS: 514/563.000; 514/567.000

L19 ANSWER 15 OF 33 USPATFULL
AN 1998:7096 USPATFULL
TI Compositions and methods for therapy and prevention of pathologies including cancer, AIDS, and anemia
IN Samid, Dvorit, Rockville, VA, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5710178 980120
AI US 95-469691 950606 (8)
RLI Division of Ser. No. US 93-135661, filed on 12 Oct 1993 which is a continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991

DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.
CLMN Number of Claims: 63
ECL Exemplary Claim: 1
DRWN 32 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 4261
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/557.000
INCLS: 514/568.000; 514/570.000
NCL NCLM: 514/557.000
NCLS: 514/568.000; 514/570.000

L19 ANSWER 16 OF 33 USPATFULL
AN 1998:4624 USPATFULL
TI Methods for promoting wound healing
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5708025 980113
AI US 95-465835 950606 (8)
RLI Division of Ser. No. US 93-135661, filed on 12 Oct 1993 which is a continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN 64 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 4206
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other

therapeutic agents. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/538.000
INCLS: 514/563.000; 514/567.000; 514/885.000; 514/886.000; 514/928.000
NCL NCLM: 514/538.000
NCLS: 514/563.000; 514/567.000; 514/885.000; 514/886.000; 514/928.000

L19 ANSWER 17 OF 33 USPATFULL
AN 97:117693 USPATFULL
TI Methods of treating rheumatoid arthritis using chimeric anti-TNF antibodies
IN Le, Junming, Jackson Heights, NY, United States
Vilcek, Jan, New York, NY, United States
Daddona, Peter, Menlo Park, CA, United States
Ghrayeb, John, Thorndale, PA, United States
Knight, David, Berwyn, PA, United States
Siegel, Scott, Westborough, MA, United States
PA New York University Medical Center, New York, NY, United States (U.S. corporation)
Centocor, Inc., Malvern, PA, United States (U.S. corporation)
PI US 5698195 971216
AI US 94-324799 941018 (8)
RLI Continuation-in-part of Ser. No. US 94-192102, filed on 4 Feb 1994 Ser. No. Ser. No. US 94-192061, filed on 4 Feb 1994, now abandoned And Ser. No. US 94-192093, filed on 4 Feb 1994, now abandoned , each Ser. No. US - which is a continuation-in-part of Ser. No. US 93-10406, filed on 29 Jan 1993, now abandoned And Ser. No. US 93-13413, filed on 2 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-943852, filed on 11 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-853606, filed on 18 Mar 1992, now abandoned which is a continuation-in-part of Ser. No. US 91-670827, filed on 18 Mar 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Lucas, John
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 33 Drawing Figure(s); 36 Drawing Page(s)
LN.CNT 5887
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-.alpha. (TNF.alpha.) and

are useful in vivo for diagnosis and therapy of a number of TNF.alpha.-mediated pathologies and conditions, including rheumatoid arthritis as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/133.100
INCLS: 424/141.100; 424/145.100; 424/192.100; 514/825.000; 530/387.300; 530/388.100; 530/388.230; 530/351.000
NCL NCLM: 424/133.100
NCLS: 424/141.100; 424/142.100; 424/145.100; 514/825.000; 530/351.000; 530/387.300; 530/388.100; 530/388.230

L19 ANSWER 18 OF 33 USPATFULL
AN 97:91647 USPATFULL
TI Oligonucleotides specific for cytokine signal transducer gp130 mRNA
IN Becherer, Kathleen Ann, San Diego, CA, United States
Dattagupta, Nanibhushan, San Diego, CA, United States
Naidu, Yathi M., Park Ridge, IL, United States
PA Gen-Probe Incorporated, San Diego, CA, United States (U.S. corporation)
PI US 5674995 971007
AI US 95-476634 950607 (8)
DT Utility
EXNAM Primary Examiner: Houtteman, Scott W.; Assistant Examiner: McGarry, Sean
LREP Cappellari, Charles B.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 791
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to oligonucleotides which are effective inhibitors of disease-associated cellular proliferation. In particular, it relates to the use of oligonulceotides which are substantially complementary to gp130 mRNA sequences. In the form of pharmaceutical compositions, these oligonucleotides are suitable for administration to human subjects for the treatment of abnormal cellular proliferation due to such diseases as cancer, autoimmune disorders and viral infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 536/024.500
INCLS: 435/006.000; 435/172.100; 514/044.000; 536/023.100; 536/024.300; 536/024.330

NCL NCLM: 536/024.500
NCLS: 435/006.000; 536/023.100; 536/024.300; 536/024.330

L19 ANSWER 19 OF 33 USPATFULL
AN 97:76161 USPATFULL
TI Methods for treating neoplastic conditions using phenylacetic acid and derivatives thereof
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5661179 970826
AI US 95-469466 950606 (8)
RLI Continuation of Ser. No. US 93-135661, filed on 12 Oct 1993 which is a continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 32 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 4056
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/538.000
INCLS: 514/563.000; 514/567.000; 560/019.000
NCL NCLM: 514/538.000
NCLS: 514/563.000; 514/567.000; 560/019.000

L19 ANSWER 20 OF 33 USPATFULL
AN 97:70718 USPATFULL
TI Methods of treating TNF-.alpha.-mediated Crohn's disease using chimeric anti-TNF antibodies
IN Le, Junming, Jackson Heights, NY, United States
Vilcek, Jan, New York, NY, United States
Dadonna, Peter, Palo Alto, CA, United States
Ghrayeb, John, Thorndale, PA, United States
Knight, David, Berwyn, PA, United States

Siegel, Scott A., Westborough, MA, United States
PA New York University Medical Center, New York, NY, United States (U.S. corporation)
Centocor, Inc., Malvern, PA, United States (U.S. corporation)
PI US 5656272 970812
AI US 94-192102 940204 (8)
RLI Continuation-in-part of Ser. No. US 93-10406, filed on 26 Jan 1993, now abandoned And Ser. No. US 93-13413, filed on 2 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-943852, filed on 11 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-853606, filed on 18 Mar 1992, now abandoned which is a continuation-in-part of Ser. No. US 91-670827, filed on 18 Mar 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Lucas, John
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 48 Drawing Figure(s); 36 Drawing Page(s)
LN.CNT 5251
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-.alpha. (TNF.alpha.) and are useful in vivo for diagnosis and therapy of a number of TNF.alpha.-mediated pathologies and conditions, including Crohn's disease, as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/133.100
INCLS: 424/145.100; 424/139.100; 435/069.100; 435/069.600; 435/069.700; 530/387.300; 530/388.230
NCL NCLM: 424/133.100
NCLS: 424/139.100; 424/145.100; 435/069.100; 435/069.600; 435/069.700; 530/387.300; 530/388.230

L19 ANSWER 21 OF 33 USPATFULL
AN 97:68500 USPATFULL
TI Methods for prevention of cancer using phenylacetic acids and derivatives thereof
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5654333 970805
AI US 95-465941 950606 (8)
RLI Division of Ser. No. US 93-135661, filed on 12 Oct 1993 which is a

continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 32 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 4088
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/538.000
INCLS: 514/563.000; 514/567.000
NCL NCLM: 514/538.000
NCLS: 514/563.000; 514/567.000

L19 ANSWER 22 OF 33 USPATFULL
AN 97:51712 USPATFULL
TI Immunosuppressant
IN Shimamura, Toshiro, Kawasaki, Japan
Nakazawa, Harumi, Kawasaki, Japan
Hamuro, Junji, Kawasaki, Japan
PA Ajinomoto Co., Inc., Tokyo, Japan (non-U.S. corporation)
PI US 5639455 970617
AI US 94-197834 940217 (8)
PRAI JP 93-28173 930217
DT Utility
EXNAM Primary Examiner: Eisenschenk, Frank C.
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1001
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Peptides which inhibit the binding of human IL-6 to human IL-6 receptor are useful as a **treatment** for **diseases** induced or aggravated by **IL-6**. DNA fragments, vectors, transformants, and methods useful for preparing such peptides are described.

Searcher : Shears 308-4994

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/133.100
INCLS: 424/130.100; 424/141.100; 424/145.100; 514/008.000; 530/387.300; 530/388.230
NCL NCLM: 424/133.100
NCLS: 424/130.100; 424/141.100; 424/145.100; 514/008.000; 530/387.300; 530/388.230

L19 ANSWER 23 OF 33 USPATFULL
AN 97:47438 USPATFULL
TI Methods for inducing differentiation of a cell using phenyacetic acid and derivatives
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5635533 970603
AI US 95-470229 950606 (8)
RLI Division of Ser. No. US 93-135661, filed on 12 Oct 1993 which is a continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 32 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 4108
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/538.000
INCLS: 514/563.000; 514/567.000
NCL NCLM: 514/538.000
NCLS: 514/563.000; 514/567.000

L19 ANSWER 24 OF 33 USPATFULL
AN 97:47437 USPATFULL
TI Compositions and methods for therapy and prevention of pathologies

including cancer, AIDS and anemia
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5635532 970603
AI US 93-135661 931012 (8)
RLI Continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.
CLMN Number of Claims: 60
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 4105
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/538.000
INCLS: 514/563.000; 514/567.000; 560/019.000
NCL NCLM: 514/538.000
NCLS: 514/563.000; 514/567.000; 560/019.000

L19 ANSWER 25 OF 33 USPATFULL
AN 97:16085 USPATFULL
TI Compositions and methods for treating and preventing pathologies including cancer
IN Samid, Dvorit, Rockville, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5605930 970225
AI US 94-207521 940307 (8)
RLI Continuation-in-part of Ser. No. US 93-135661, filed on 12 Oct 1993 which is a continuation-in-part of Ser. No. US 91-779744, filed on 21 Oct 1991
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
LREP Needle & Rosenberg, P.C.

CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 60 Drawing Figure(s); 43 Drawing Page(s)
LN.CNT 7722
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods of treating anemia, cancer, AIDS, or severe .beta.-chain hemoglobinopathies by administering a therapeutically effective amount of phenylacetate or pharmaceutically acceptable derivatives thereof or derivatives thereof alone or in combination or in conjunction with other therapeutic agents including retinoids, hydroxyurea, and flavonoids. Intravesicle methods of treatment of cancers phenylacetate. Pharmacologically-acceptable salts alone or in combinations and methods of preventing AIDS and malignant conditions, and inducing cell differentiation are also aspects of this invention. A product as a combined preparation of phenylacetate and a retinoid, hydroxyurea, or flavonid (or other mevalonate pathway inhibitor) for simultaneous, separate, or sequential use in treating a neoplastic condition in a subject. Methods of modulating lipid metabolism and/or reducing serum triglycerides in a subject using phenylacetate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/510.000
INCLS: 514/513.000; 514/515.000; 514/529.000; 514/538.000; 514/563.000; 514/567.000
NCL NCLM: 514/510.000
NCLS: 514/513.000; 514/515.000; 514/529.000; 514/538.000; 514/563.000; 514/567.000

L19 ANSWER 26 OF 33 USPATFULL
AN 97:1546 USPATFULL
TI Interleukin-6 receptor antagonists
IN Brakenhoff, Just P. J., Amsterdam, Netherlands
Aarden, Lucien A., Broek in Waterland, Netherlands
PA Cetus Oncology Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5591827 970107
AI US 94-357538 941216 (8)
RLI Continuation of Ser. No. US 92-959942, filed on 20 Oct 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Ulm, John; Assistant Examiner: Mertz, Prema
LREP Rin-Laures, Li-Hsien; Savereide, Paul B.; Blackburn, Robert P.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1356
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a class of interleukin-6 (IL-6) muteins which act as IL-6 receptor antagonists, thereby inhibiting the normal function of naturally-occurring IL-6. These IL-6 receptor antagonists are preferably IL-6 molecules containing one or more mutations in the Site II region comprising amino acids 154-163. This invention also provides pharmaceutical compositions comprising IL-6 receptor antagonists with a pharmaceutically acceptable carrier. This invention further provides methods for **treating** IL-6 related **diseases** such as sepsis and multiple myeloma, the methods comprising administering to a patient an IL-6 receptor antagonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/351.000
INCLS: 435/069.200; 424/085.200; 930/141.000
NCL NCLM: 530/351.000
NCLS: 424/085.200; 435/069.520; 930/141.000

L19 ANSWER 27 OF 33 USPATFULL
AN 96:101285 USPATFULL
TI Anti-gp130 **monoclonal** antibodies
IN Burstein, Samuel A., Edmond, OK, United States
PA The Board Of Regents Of The University Of Oklahoma, Norman, OK, United States (U.S. corporation)
PI US 5571513 961105
AI US 95-455799 950531 (8)
DT Utility
EXNAM Primary Examiner: Budens, Robert D.; Assistant Examiner: Reeves, Julie E.
LREP Dunlap & Codding, P.C.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 781
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Anti-gp130 **monoclonal** antibodies (**Mabs**) obtained from hybridomas designated 4B11 and 2H4 are effective in the inhibition of the acute phase response on hepatoma cells and prevent the IL-6-induced growth inhibition of A375 cells in vitro. Administration of the antibodies to dogs showed that 2H4 is a potent in vivo inhibitor of the IL-6-induced acute phase response, abrogating IL-6-mediated-increments in fibrinogen, C-reactive protein and the platelet count. Antibodies may be used in methods for measuring soluble gp130 and in therapeutic treatments. The 2H4 antibody may be used in inhibiting in vivo the function of gp130 or cellular factors dependent on gp130 for cellular transduction.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/144.100

INCLS: 424/153.100; 424/173.100; 435/070.210; 435/172.200; 435/240.270; 530/387.100; 530/388.220; 530/388.700; 530/388.850; 530/391.300; 530/389.600
NCL NCLM: 424/144.100
NCLS: 424/153.100; 424/173.100; 435/070.210; 435/334.000; 530/387.100; 530/388.220; 530/388.700; 530/388.850; 530/389.600; 530/391.300

L19 ANSWER 28 OF 33 USPATFULL
AN 96:53064 USPATFULL
TI Human interleukin 6 inhibitor
IN Penza, Delia E., Alamo, CA, United States
Faris, Susan K., San Francisco, CA, United States
Lembach, Kenneth J., Danville, CA, United States
PA Bayer Corporation, Berkeley, CA, United States (U.S. corporation)
PI US 5527546 960618
AI US 94-288516 940810 (8)
DT Utility
EXNAM Primary Examiner: Wityshyn, Michael G.; Assistant Examiner: Witz, Jean C.
LREP Giblin, James A.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 500
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A previously undescribed Interleukin-6 inhibitor activity has been successfully isolated from the supernatant of the human promyelocytic leukemia cell line HL-60. Treatment of the HL-60 cell line with cycloheximide prevents the appearance of the inhibitory activity in the cellular supernatant. Incubation of the HL-60 supernatant with trypsin destroys the activity. The above observations indicate the inhibitor is a protein. Membrane and gel filtration studies indicate the protein has a molecular weight between 10,000 and 30,000 daltons. The inhibitor was partially isolated from other proteins by dye-ligand and reverse phase chromatography.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/573.000
NCL NCLM: 424/573.000

L19 ANSWER 29 OF 33 USPATFULL
AN 95:105942 USPATFULL
TI CNTF and IL-6 antagonists
IN Stahl, Neil, Carmel, NY, United States
Economides, Aris N., New York, NY, United States
Yancopoulos, George D., Yorktown Heights, NY, United States
PA Regeneron Pharmaceuticals, Inc., Tarrytown, NY, United States

(U.S. corporation)
PI US 5470952 951128
AI US 93-140222 931020 (8)
DT Utility
EXNAM Primary Examiner: Draper, Garnette D.; Assistant Examiner: Cermak, Shelly Guest
LREP Kempler, Gail M.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 672
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Heterodimer proteins comprising a soluble .alpha. specificity determining cytokine receptor component and the extracellular domain of a .beta. receptor component function as CNTF and IL-6 antagonsists.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/350.000
INCLS: 530/351.000; 530/399.000; 530/402.000; 424/085.200
NCL NCLM: 530/350.000
NCLS: 424/085.200; 530/351.000; 530/399.000; 530/402.000

L19 ANSWER 30 OF 33 USPATFULL
AN 95:54319 USPATFULL
TI DNA encoding a fusion receptor for oncostatin M and leukemia inhibitory factor
IN Gearing, David P., Seattle, WA, United States
PA Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI US 5426048 950620
AI US 93-115370 930831 (8)
RLI Continuation of Ser. No. US 91-797556, filed on 22 Nov 1991, now patented, Pat. No. US 5262522
DT Utility
EXNAM Primary Examiner: Draper, Garnette D.; Assistant Examiner: Ulm, John D.
LREP Seese, Kathryn A.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 13 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 2172
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A receptor protein comprising a gp130 polypeptide linked to a single-chain leukemia inhibitory factor receptor (LIF-R) polypeptide is capable of binding both oncostatin M and leukemia inhibitory factor (LIF). The receptor protein binds LIF with greater affinity than does the single-chain LIF-R polypeptide alone. The receptor may be produced as a fusion protein in recombinant cells. The gp130 polypeptide binds oncostatin M, but

with lower affinity than does the inventive receptor protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/252.300
INCLS: 435/069.700; 435/320.100; 536/023.400
NCL NCLM: 435/252.300
NCLS: 435/069.700; 435/320.100; 536/023.400

L19 ANSWER 31 OF 33 USPATFULL
AN 95:9803 USPATFULL
TI Tumor necrosis factor-induced protein TSG-6
IN Lee, Tae H., Piscataway, NJ, United States
Wisniewski, Hans-Georg, Spring Valley, NY, United States
Vilcek, Jan, New York, NY, United States
PA New York University, New York, NY, United States (U.S. corporation)
PI US 5386013 950131
AI US 93-24868 930301 (8)
RLI Continuation of Ser. No. US 91-642312, filed on 14 Jan 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Draper, Garnette D.; Assistant Examiner: Kemmerer, Elizabeth C.
LREP Browdy and Neimark
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 50 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 2952
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Pleiotropic pro-inflammatory cytokines, such as TNF and IL-1, induce expression of a protein molecule, termed TSG-6, in connective tissue cells. The TSG-6 protein and functional derivatives thereof, DNA coding therefor, expression vehicles, such as a plasmids, and host cells transformed or transfected with the DNA molecule, and methods for producing the protein and the DNA are provided. Antibodies specific for the TSG-6 protein are disclosed, as is a method for detecting the presence of TSG-6 protein in a biological sample, using the antibody or another molecule capable of binding to TSG-6 such as hyaluronic acid. A method for detecting the presence of nucleic acid encoding a normal or mutant TSG-6 protein, a method for measuring induction of expression of TSG-6 in a cell using either nucleic acid hybridization or immunoassay, a method for identifying a compound capable of inducing the expression of TSG-6 in a cell, and a method for measuring the ability of a cell to respond to TNF are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/350.000

INCLS: 435/069.100; 530/351.000
NCL NCLM: 530/350.000
NCLS: 435/069.100; 530/351.000

L19 ANSWER 32 OF 33 USPATFULL
AN 93:104817 USPATFULL
TI Cancer-associated SCM-recognition factor, preparation and method of use
IN Cercek, Boris, 4318 Camphor Ave., Yorba Linda, CA, United States 92686
Cercek, Lea, 4318 Camphor Ave., Yorba Linda, CA, United States 92686
PI US 5270171 931214
AI US 90-539686 900618 (7)
RLI Continuation-in-part of Ser. No. US 88-167007, filed on 3 Mar 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-22759, filed on 6 Mar 1987, now abandoned
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Preston, D. R.
LREP Sheldon & Mak]>
CLMN Number of Claims: 68
ECL Exemplary Claim: 1,33
DRWN 5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 4236
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cancer recognition factor (SCM factor) useful in the performance of the structuredness of the cytoplasmic matrix (SCM) test has been isolated, purified to substantial homogeneity, and characterized, and methods for its use have been described. The factor is a peptide of at least 9 amino acid residues including a core sequence of 9 amino acid residues having an amphipathicity profile substantially equivalent to that of the sequence F-L-M-I-D-Q-N-T-K and produces at least a 10 percent decrease in the intracellular fluorescence polarization value of SCM-responding lymphocytes from donors afflicted with cancer. A synthetic SCM factor representing a consensus sequence of M-I-P-P-E-V-K-F-N-K-P-F-V-F-L-M-I-D-Q-N-T-K-V-P-L-F-M-G-K is fully active. Antibodies specific for SCM factor are useful in immunoassays that can detect the factor, including detection in cancer cells grown in vitro. The SCM factor is useful for screening of blood samples and other body fluids or cell aspirates for the presence of malignancy in the donor. The multiple action spectrum of the SCM factor including cancer proliferation and invasion promotion, as well as inhibition of the host's immune defense mechanisms and synthesis of SCM factor by cancer cells, represents a novel target for cancer management. Methods for reducing in vivo activity of the SCM factor, such as dialysis or antibody neutralization, can also be useful in the management of

cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/029.000
INCLS: 436/811.000; 436/813.000; 530/328.000; 530/327.000; 530/326.000; 530/325.000; 530/324.000; 530/350.000; 530/380.000
NCL NCLM: 435/029.000
NCLS: 436/811.000; 436/813.000; 530/324.000; 530/325.000; 530/326.000; 530/327.000; 530/328.000; 530/350.000; 530/380.000

L19 ANSWER 33 OF 33 USPATFULL
AN 93:96237 USPATFULL
TI Receptor for oncostatin M and leukemia inhibitory factor
IN Gearing, David P., Seattle, WA, United States
PA Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI US 5262522 931116
AI US 91-797556 911122 (7)
DT Utility
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Ulm, John D.
LREP Seese, Kathryn A.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 2133
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A receptor protein comprising a gp130 polypeptide linked to a single-chain leukemia inhibitory factor receptor (LIF-R) polypeptide is capable of binding both oncostatin M and leukemia inhibitory factor (LIF). The receptor protein binds LIF with greater affinity than does the single-chain LIF-R polypeptide alone. The receptor may be produced as a fusion protein in recombinant cells. The gp130 polypeptide binds oncostatin M, but with lower affinity than does the inventive receptor protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/350.000
INCLS: 435/069.700; 435/252.300; 435/370.100
NCL NCLM: 530/350.000
NCLS: 435/069.700; 435/252.300; 435/320.100

=> d his l20-

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGB' ENTERED AT 15:06:35 ON 15 JAN 1999)
L20 99 S L15

L21 99 S L20 NOT L7
L22 21 S L21 AND ADMIN?
L23 12 DUP REM L22 (9 DUPLICATES REMOVED)

=> d 1-12 bib abs

L23 ANSWER 1 OF 12 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 98-10488 BIOTECHDS
TI Treatment of multiple myeloma and **monoclonal** myopathy with anti-viral agent;
in the form of antisense molecule or **monoclonal** antibody to treat, prevent or vaccinate against e.g. multiple myeloma, Alzheimer disease, systemic lupus erythematosus, scleroderma, and cancer
AU Berenson J R; Rettig M B; Vescio R A
PA Berenson J R; Rettig M B; Vescio R A
LO Los Angeles, CA, USA.
PI WO 9835684 20 Aug 1998
AI WO 98-US2820 12 Feb 1998
PRAI US 97-967504 11 Nov 1997; US 97-800710 14 Feb 1997
DT Patent
LA English
OS WPI: 98-480765 [41]
AN 98-10488 BIOTECHDS
AB A method of **treating** a patient with multiple myeloma (MM) or **monoclonal** gammopathy of undetermined significance (MGUS) is claimed, involving **administration** of a virucide that is effective against Kaposi's sarcoma-associated herpes-like Virus (KSHV). Also claimed is a method of **treating** KSHV- and Interleukin (**IL**)-**6** associated **disease**. The virucide can be an inhibitory nucleic acid, e.g. an antisense molecule, that inhibits the replication or expression of KSHV. Alternatively the virucide can be an antibody, either **monoclonal** or polyclonal, that blocks KSHV replication or expression. Either of these can be conjugated with an anti-viral or chemotherapeutic agent. Also claimed is a method of vaccinating against KSHV a or **IL-6** associated **disease** by **administration** of a KSHV-specific immunogen. A method of determining the efficacy of a **therapy** in patients with MM, MGUS, and KSHV or **IL-6** associated **disorders** by detecting KSHV-specific nucleic acid or protein sequences. This can also be used to detect KSHV in patients, and to **treat** or prevent MGUS, MM, Alzheimer disease, multiple sclerosis, rheumatoid arthritis, etc. (135pp)

L23 ANSWER 2 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 2
AN 1998174733 EMBASE
TI In vivo blocking effects of a humanized antibody to human

interleukin-6 receptor on interleukin-6 function in primates.
AU Shinkura H.; Imazeki I.; Yamazaki M.; Oda Y.; Kotoh M.; Mihara M.
CS H. Shinkura, Fuji-Gotemba Research Laboratories, Chugai Pharmaceutical Co. Ltd., 1-135 Komakado, Gotemba-shi, Shizuoka 412, Japan
SO Anticancer Research, (1998) 18/2 A (1217-1221).
Refs: 38
ISSN: 0250-7005 CODEN: ANTRD4
CY Greece
DT Journal; Article
FS 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB A humanized antibody to human interleukin-6 (IL-6) receptor, MRA, which was constructed by grafting the complementary determining regions, is expected to be useful as a **therapeutic** agent for **IL-6**-related **diseases**, especially multiple myeloma. We examined the ability of MRA to block the in vivo function of IL-6 and its serum concentration profile in primates. Cynomolgus monkeys were intravenously **administered** with MRA at doses of 0 (vehicle) or 5 mg/kg, then subcutaneously injected with human IL-6 at a dose of 5 .mu.g/kg, once a day for 7 days. The injections of IL-6 increased blood platelet counts two-fold and elevated serum C-reactive protein levels to 0.15 to 0.17 mg/ml. These IL-6-induced typical responses were completely inhibited by single pretreatment with MRA. Serum concentrations of MRA were maintained for a long period; some even at one week after **administration**, were regarded as having sufficient levels to inhibit the myeloma cell growth. These findings suggest that MRA may be effective in the **treatment** of **IL-6** -related **diseases**.

L23 ANSWER 3 OF 12 MEDLINE
AN 1998027790 MEDLINE
DN 98027790
TI Modulation of chronic excessive interleukin-6 production in multiple myeloma does not affect thyroid hormone concentrations.
AU van Zaanen H C; Romijn J A; Sauerwein H P; Lokhorst H M; Warnaar S O; Aarden L A; Endert E; van Oers M H
CS Department of Hematology, University of Amsterdam, The Netherlands.
SO METABOLISM: CLINICAL AND EXPERIMENTAL, (1997 Nov) 46 (11) 1343-8.
Journal code: MUM. ISSN: 0026-0495.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

Searcher : Shears 308-4994

EM 199802
EW 19980204
AB Interleukin-6 (IL6) is believed to be involved in alterations of thyroid hormone metabolism in acute nonthyroidal illness. To evaluate the effects of IL6 on thyroid hormone metabolism in a chronic **IL6**-mediated **disease**, we measured thyroid hormone concentrations in multiple myeloma patients **treated** with intravenous anti-IL6 chimeric **monoclonal** antibodies ([cMabs] Kd = 6.25 x 10(-12) mol/L). Twelve patients were studied, receiving at least one complete **treatment** cycle of 14 days (daily dose: 5 mg, n = 3; 10 mg, n = 3; 20 mg, n = 3; and 40 mg, n = 3). Eight of them also completed a second **treatment** cycle of 14 days. Thyroid hormone concentrations were measured before, during, and after **treatment** with the anti-IL6 cMab. Even in the group with the lowest dosage, IL6 activity measured by the B9 bioassay was blocked completely. Compared with the reference ranges, 10 of 12 patients had one or more abnormal pretreatment values for thyroid hormone concentrations. Thyroid autoantibodies were negative in all patients. There was no correlation between thyroid hormone concentrations and IL6 levels, although plasma IL6 levels were increased in all but one subject. Moreover, neutralization of free IL6 by the anti-IL6 cMab did not affect thyroid hormone concentrations, although IL6-dependent C-reactive protein (CRP) levels decreased to undetectable levels in 11 of 12 patients. Two patients developed infectious complications resulting in increased free IL6 and CRP levels and in profound alterations of thyroid hormone levels consistent with an acute euthyroid sick syndrome. We conclude that IL6 is not a major determinant of thyroid hormone abnormalities in a chronic **disease** like multiple myeloma, but **IL6** may be involved in thyroid hormone metabolism in acute diseases (probably in combination with other factors).

L23 ANSWER 4 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 3
AN 1997:488041 BIOSIS
DN PREV199799787244
TI Safety and kinetic properties of a humanized antibody to human interleukin-6 receptor in healthy non-human primates.
AU Shinkura, Hirofumi (1); Imazeki, Ikuo; Fukushima, Naoshi; Chiba, Nobuyuki; Takahashi, Fumiaki; Aikawa, Hitoshi; Kitamura, Hidetomo; Furuichi, Tastuya; Horiba, Naoshi; Ohsugi, Yoshiyuki
CS (1) Fuji-Gotemba Res. Lab., Chugai Pharmaceutical Co. Ltd., 1-135 Komakado, Gotemba-shi, Shizuoka 412 Japan
SO Toxicology, (1997) Vol. 122, No. 3, pp. 163-170.
ISSN: 0300-483X.
DT Article
LA English
AB A **monoclonal** antibody, hPM-1, was constructed by grafting the complementarity determining regions to human interleukin-6

(IL-6) receptor, raised in mouse, onto a human antibody backbone (humanized antibody). It is expected to be useful as a **therapeutic** agent for **IL-6**-related **diseases** such as multiple myeloma. To investigate the toxicological and kinetic properties of hPM-1 preliminarily, normal cynomolgus monkeys, which showed cross-reactivity with hPM-1, were intravenously **administered** with hPM-1 at doses of 0 (vehicle), 4 or 40 mg/kg once a week for 13 weeks. Upon toxicological examination, there were no changes in clinical signs, food consumption, body weights, urinalyses, body temperatures, electrocardiograms, hematological and biochemical parameters including blood platelet counts, serum levels of immunoglobulin G and C-reactive protein, and pathological findings. In a kinetic study, serum concentrations of hPM-1 showed a linearity between doses of 4 and 40 mg/kg. The serum concentrations, even at a dose of 4 mg/kg, were maintained at a high enough level to inhibit the IL-6 functions throughout the period of the study. Concentrations of hPM-1 in bone marrow were almost equal to those in serum. The antibodies against hPM-1 were detected only in one of four monkeys receiving hPM-1. This study suggests that blockage of the IL-6 receptor by hPM-1 does not induce any influence on a healthy living body, and hPM-1 is not toxic under the conditions of this investigation.

L23 ANSWER 5 OF 12 MEDLINE
AN 96433569 MEDLINE
DN 96433569
TI Coadministration of interleukin-6 (IL-6) and soluble IL-6 receptor delays progression of wobbler mouse motor neuron disease.
AU Ikeda K; Kinoshita M; Tagaya N; Shiojima T; Taga T; Yasukawa K; Suzuki H; Okano A
CS Fourth Department of Internal Medicine, Toho University Ohashi Hospital, Tokyo, Japan.
SO BRAIN RESEARCH, (1996 Jul 8) 726 (1-2) 91-7.
Journal code: B5L. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
AB Interleukin-6 (IL-6), a multipotential cytokine, initiates signal transduction pathways similar to those of ciliary neurotrophic factor (CNTF) and leukemia inhibitory factor (LIF). These molecules share the signal transducing receptor component, gp130. IL-6 triggers homodimerization of gp130, whereas CNTF and LIF induce heterodimerization of gp130 and LIF receptor. Although CNTF or LIF **treatment** attenuates motor deficits in wobbler mouse motor neuron **disease** (MND), neuroprotective effects of **IL-6** on this animal have not yet been clarified.

Searcher : Shears 308-4994

Here we studied whether simultaneous **treatment** with IL-6 and soluble IL-6 receptor (sIL-6R) can ameliorate symptomatic and neuropathological changes in wobbler mouse MND. After clinical diagnosis at postnatal age 3-4 weeks, wobbler mice received subcutaneous injection with human recombinant IL-6 (1.0 mg/kg), human sIL-6R (0.5 mg/kg), IL-6 + sIL-6R or vehicle, daily for 4 weeks in a blind fashion. Compared to vehicle, coadministration with IL-6 and sIL-6R potentiated grip strength, attenuated muscle contractures in the forelimbs, reduced denervation muscle atrophy and prevented degeneration of spinal motor neurons. Single **administration** with IL-6 or sIL-6R did not retard the symptomatic and neuropathological progression, although IL-6-**treated** mice did not raise anti-IL-6 antibodies. **Treatment** with IL-6 + sIL-6R, but not with IL-6 or sIL-6R alone delayed progression of wobbler mouse MND. Our results indicate that the neuroprotective mechanism for IL-6/sIL-6R on wobbler mouse MND differs from that of CNTF or LIF alone. We hypothesize that IL-6/sIL-6R complex may function on motor neurons through activation and homodimerization of gp130.

L23 ANSWER 6 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 95064730 EMBASE
TI Pharmacokinetic study of anti-interleukin-6 (IL-6) therapy with **monoclonal** antibodies: Enhancement of IL-6 clearance by cocktails of anti-IL-6 antibodies.
AU Montero-Julian F.A.; Klein B.; Gautherot E.; Brailly H.
CS Immunotech S.A., 130, Avenue de Lattre de Tassigny, 13276 Marseille Cedex 09, France
SO Blood, (1995) 85/4 (917-924).
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal
FS 025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB The use of inhibiting cytokine-binding-proteins (CBPs) such as soluble cytokine receptors and anticytokine antibodies is considered for the **treatment** of cytokine-dependent **diseases**. The pleiotropic cytokine **interleukin-6** (**IL-6**) is a target for immunointervention in numerous pathologic situations, including multiple myeloma, B-cell lymphoma, and rheumatoid arthritis. An antitumor response was obtained in the **treatment** of a patient with multiple myeloma. A controversial issue is to evaluate whether the carrier effect of the CBPs might limit their efficiency in blocking the target cytokine. We analyzed the pharmacokinetics of radiolabeled IL-6 in mice **treated** with various combinations of

anti-IL-6 antibodies. We show that injection of one or two antibodies led to the stabilization of the cytokine. Conversely, simultaneous **treatment** with three anti-IL-6 antibodies, binding to three distinct epitopes, induced the rapid uptake of the trimeric immune complexes by the liver and the elimination of IL-6 from the central compartment. The use of cocktails of three antibodies binding simultaneously to a cytokine thus provides a new means of enhancing the clearance of the target molecule and should help in the design of antibody-based clinical trials by overcoming the problem of the accumulation of the cytokine in the form of monomeric immune complexes.

L23 ANSWER 7 OF 12 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 94:299120 SCISEARCH
GA The Genuine Article (R) Number: NK795
TI INTERLEUKIN-6 EXACERBATES GLOMERULONEPHRITIS IN (NZBXNZW)F-1 MICE
AU RYFFEL B (Reprint); CAR B D; GUNN H; ROMAN D; HIESTAND P; MIHATSCH M J
CS UNIV ZURICH, FAC MED, INST TOXICOL, CH-8603 SCHWERZENBACH 1ZSCHWERZENB, SWITZERLAND (Reprint); SANDOZ PHARMA INC, E HANOVER, NJ, 00000; SANDOZ PHARMA AG, BASEL, SWITZERLAND; UNIV BASEL, INST PATHOL, BASEL, SWITZERLAND
CYA SWITZERLAND; USA
SO AMERICAN JOURNAL OF PATHOLOGY, (MAY 1994) Vol. 144, No. 5, pp. 927-937.
ISSN: 0002-9440.
DT Article; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 56
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The ability of interleukin-6 (IL-6) to modulate immune parameters and mesangial cell function suggests a role for this cytokine in the development of autoimmune glomerulonephritis. This hypothesis was tested in 6-month-old female (NZBxNZW)F-1 mice that were **administered** recombinant human IL-6 (rhIL-6) (50 and 250 mu/kg s.c.) for 12 weeks, resulting in an accelerated and severe form of membranoproliferative glomerulonephritis associated with marked upregulation of mesangial major histocompatibility complex class II antigen and glomerular ICAM-1 expression. To distinguish direct effects of rhIL-6 on the renal mesangium from those mediated through the immune system, (NZBxNZW)F-1 mice were immunosuppressed with cyclosporin. Immunosuppression by cyclosporin inhibited the development by cyclosporin inhibited the development of glomerulonephritis, decreased class II antigen expression, and abrogated IL-6-mediated effects. **Administration** of neutralizing anti-IL-6 antibody had no effect on the spontaneous development of glomerulonephritis in (NZBxNZW)F-1 mice. This finding, together with undetectable IL-6 serum levels, makes a

pathogenetic role of endogenously produced **IL-6** in this **disease** model unlikely. In contrast to (NZBxNZW)F-1 mice, parental NZW or BALB/c mice given high doses of rhIL-6 (500 mu g/kg) or recombinant murine IL-6 (100 mu g/kg) daily for 4 weeks failed to develop morphological or biochemical evidence of glomerulonephritis. Induction of acute phase proteins, anemia, thrombocytosis, and induction of renal class II antigen confirmed the biological activity of IL-6 in these mice. In conclusion, while non-nephritogenic in normal mice, IL-6 accelerates the development of the genetically determined glomerulonephritis of (NZBxNZW)F-1 mice through effects mediated by a modulated immune system. Since neutralizing IL-6 antibody **treatment** did not prevent the development of glomerulonephritis, it is unlikely that increased IL-6 production plays a role in the pathogenesis of lupus nephritis.

L23 ANSWER 8 OF 12 TOXLINE
AN 1995:246995 TOXLINE
DN IPA-94-1060092
TI Brief report: alleviation of systemic manifestations of Castleman's disease by **monoclonal** anti-interleukin-6 antibody.
AU Beck J T; Hsu S M; Wijdenes J; Bataille R; Barlogie B; et al
CS Univ. of Arkansas for Med. Sci., Slot 508, 4301 W. Markham, Little Rock, AR 72205, USA.
SO N. Engl. J. Med, (1994). Vol. 330, Mar 3, pp. 602-605 (REF 15). CODEN: NEJMAG. ISSN: 0028-4793.
FS IPA
LA English
OS IPA 31-1060092
EM 199507
AB IPA COPYRIGHT: ASHP The use of anti-interleukin 6 **monoclonal** antibody (BE-8) in the **treatment** of a 27-yr-old man with Castleman's **disease** and elevated serum **interleukin** 6 concentration who received intravenous BE-8 **monoclonal** antibody at a dose of 40 mg/day **administered** over 1 h for 2 days, followed by daily doses of 10 mg for 82 days is reported. The symptoms and signs of disease resolved, and most of the abnormal laboratory values improved dramatically within a few days, but the abnormality returned on cessation of **therapy**. Because of persistent mesenteric mass, the patient was **treated** with high dose dexamethasone. Ultimately, the mass was resected, resulting in a sustained remission of all clinical and biochemical manifestations of the disease.

L23 ANSWER 9 OF 12 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 92-05868 BIOTECHDS
TI New **monoclonal** antibody and hybridoma; against human **B**-cell **differentiation factor**; use in **therapy** of autoimmune

disease, etc., or as antiinflammatory
PA Ajinomoto
PI JP 04008296 13 Jan 1992
AI JP 90-107863 24 Apr 1990
PRAI JP 90-107863 24 Apr 1990
DT Patent
LA Japanese
OS WPI: 92-061717 [08]
AN 92-05868 BIOTECHDS
AB A new **monoclonal** antibody (**MAb**) inhibits binding of human B-cell differentiation factor (hBCDF) and hBCDF receptor (hBCDFR), and neutralizes the biological activity of hBCDF. The **MAb** is produced by hybridoma FERM P-11406 cell culture. The **MAb** (e.g. 1-39) is produced by immunization of a mouse with hBCDFR expressing cells as an immunogen (e.g. human myeloma U266 cells). The **MAb** is useful in therapy of autoimmune disease, immunodeficiency or inflammation, e.g. rheumatoid arthritis, systemic lupus erythematosus, etc., which is characterized by production of excess hBCDF. In an example, 6- to 8-wk-old female BALB/c mice were immunized with U266 cells. Spleen cells from the immunized mice were fused with an X63-Ag8.653 cell culture in the presence of 50% PEG 4,000. Hybridoma 1-39 contained the desired activity, and was **administered** i.p. to a BALB/c mouse to form ascites fluid, from which the **MAb** was then purified. (7pp)

L23 ANSWER 10 OF 12 MEDLINE
AN 92347391 MEDLINE
DN 92347391
TI Anti-human interleukin-6 receptor antibody inhibits human myeloma growth in vivo.
AU Suzuki H; Yasukawa K; Saito T; Goitsuka R; Hasegawa A; Ohsugi Y; Taga T; Kishimoto T
CS Biotechnology Research Laboratory, Tosoh Corporation, Kanagawa, Japan.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1992 Aug) 22 (8) 1989-93. Journal code: EN5. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199211
AB Myeloma is one of the interleukin (**IL**)-**6**-related **diseases** to which abnormal expression of **IL**-**6** has been reported to be linked. We examined the in vivo inhibitory effect of anti-human IL-6 receptor (IL-6R) antibody on human myeloma cell growth in mice. SCID mice were subcutaneously inoculated with solid tumor of the myeloma cell line S6B45 in which human IL-6 was acting as an autocrine growth factor. Ten

intraperitoneal **administrations** of 100 micrograms of the anti-human IL-6R antibody PM1 at 48-h intervals strongly inhibited the growth of S6B45 cells when the **administration** started 24 h after tumor inoculation. The tumor growth inhibition in vivo was also observed by **administration** of the anti-human IL-6 antibody MH166 using the same procedure as for PM1. The inhibitory effect of PM1 was not significant when the **administration** started 5 or more days after tumor inoculation. This work indicates that anti-human IL-6R antibody, as well as anti-human IL-6 antibody inhibits human myeloma growth in vivo, and provides an animal model for testing the **therapeutic** value of agents such as antibodies to human IL-6, IL-6R and gp130, an IL-6R-associated signal transducer, in the **treatment** of human myelomas.

L23 ANSWER 11 OF 12 BIOTECHDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 91-08267 BIOTECHDS
TI Interleukin-6 **monoclonal** antibody and hybridoma cell lines;
application in **therapy**, prophylaxis and diagnosis of **IL-6** related **diseases**
PA Centre-Reg.Transfus.Sanguine
PI DE 3939706 21 Mar 1991
AI DE 89-939706 1 Dec 1989
PRAI DE 89-939706 1 Dec 1989
DT Patent
LA German
OS WPI: 91-081550 [12]
AN 91-08267 BIOTECHDS
AB Hybridoma cell lines CNCM 1/913 (BE-8), 1/911 (BE-4) and 1/912 (BF-6) produce **monoclonal** antibodies (**MAbs**) specific for different epitopes of the human interleukin-6 (IL-6) molecule. The hybridoma cell lines are obtained by fusion of IL-6-immunized mouse spleen cells and mouse myeloma cells. The **MAbs** may be used in **therapy**, prophylaxis, and diagnosis of **IL-6**-related **diseases** e.g. autoimmune **disease**, infections of all kinds, tumors, etc. The **MAbs** may be used in **therapy** of multiple myeloma, myeloic leukemia, Kastleman syndrome, systemic lupus erythematosus, kidney cell carcinoma, inflammatory arthropathy, etc. Low doses (0.5-5 mg/ml, preferably 1 mg/ml) are **administered** systemically without producing side effects. Local application may be possible. In an example, BE-4, BE-8, BF-6 reduced binding of IL-6 to receptors on U226 cells to a level of 11%, 14% and 92%, respectively. Thus BE-4 and BE-8 are IL6-inhibitors. (8pp)

L23 ANSWER 12 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 91320041 EMBASE
TI Murine anti-interleukin-6 **monoclonal** antibody therapy for

a patient with plasma cell leukemia.

AU Klein B.; Wijdenes J.; Zhang X.-G.; Jourdan M.; Boiron J.-M.; Brochier J.; Liautard J.; Merlin M.; Clement C.; Morel-Fournier B.; Lu Z.-Y.; Mannoni P.; Sany J.; Bataille R.
CS INSERM U291, Zolad, 99 Rue Puech Villa, 34080 Montpellier, France
SO BLOOD, (1991) 78/5 (1198-1204).
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal
FS 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
AB A patient with primary plasma cell leukemia resistant to chemotherapy was **treated** for 2 months with daily intravenous injections of anti-interleukin-6 (IL-6) **monoclonal** antibodies (**MoAbs**). The patient's clinical status improved throughout the **treatment** and no major side effects were observed. Serial monitoring showed blockage of the myeloma cell proliferation in the bone marrow (from 4.5% to 0% myeloma cells in the S-phase in vivo) as well as reduction in the serum calcium, serum **monoclonal** IgG, and the serum C-reactive protein levels. The serum calcium and serum **monoclonal** IgG corrected by approximately 30%, whereas the C-reactive protein corrected to undetectable levels during **treatment**. No major side effects developed, although both platelet and circulating neutrophil counts decreased during anti-IL-6 **therapy**. A transient immunization was detected 15 days after the initiation of the **treatment**, which could explain the recovery of myeloma cell proliferation after 2 months of **treatment** (2% myeloma cells in the S phase). In conclusion, this first anti-IL-6 clinical trial demonstrated the feasibility of injecting anti-IL-6 **MoAbs**, and also a transient tumor cytostasis and a reduction in IL-6-related toxicities. It gave insight into the major biologic activities of IL-6 in vivo and may serve as a basis for further development of anti-IL-6 **therapy** in myeloma and other **IL-6** -related **diseases**.

=> d his l24-; d 1-23 bib abs; fil hom

(FILE 'CAPLUS, BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGB, USPATFULL' ENTERED AT 15:28:14 ON 15 JAN 1999)

L24 9878 S KISHIMOTO T?/AU
L25 92 S KATSUME A?/AU
L26 34609 S SAITO H?/AU
L27 2 S L24 AND L25 AND L26

Authors

Searcher : Shears 308-4994

L28 65 S L24 AND (L25 OR L26)
L29 38 S L25 AND L26
L30 101 S L27 OR L28 OR L29
L31 23 DUP REM L30 (78 DUPLICATES REMOVED)

L31 ANSWER 1 OF 23 CAPLUS COPYRIGHT 1999 ACS
AN 1999:19301 CAPLUS
TI Accelerated apoptosis of lymphocytes by augmented induction of Bax in SSI-1 (STAT-induced STAT inhibitor-1) deficient mice
AU Naka, Tetsuji; Matsumoto, Tomoshige; Narazaki, Masashi; Fujimoto, Minoru; Morita, Yoshiaki; Ohsawa, Yoshiyuki; **Saito, Hiroshi** ; Nagasawa, Takashi; Uchiyama, Yasuo; **Kishimoto, Tadamitsu**
CS Department of Medicine III, Osaka University Medical School, Suita, 565-0871, Japan
SO Proc. Natl. Acad. Sci. U. S. A. (1998), 95(26), 15577-15582
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Growth, differentiation, and programmed cell death (apoptosis) are mainly controlled by cytokines. The Janus kinase-signal transducers and activators of transcription (JAK-STAT) signal pathway is an important component of cytokine signaling. We have previously shown that STAT3 induces a mol. designated as SSI-1, which inhibits STAT3 functions. To clarify the physiol. roles of SSI-1 in vivo, we generated, here, mice lacking SSI-1. These SSI-1-/- mice displayed growth retardation and died within 3 wk after birth. Lymphocytes in the thymus and spleen of the SSI-1-/- mice exhibited accelerated apoptosis with aging, and their no. was 20-25% of that in SSI-1+/+ mice at 10 days of age. However, the differentiation of lymphocytes lacking SSI-1 appeared to be normal. Among various pro- and anti-apoptotic mols. examd., an up-regulation of Bax was found in lymphocytes of the spleen and thymus of SSI-1-/- mice. These findings suggest that SSI-1 prevents apoptosis by inhibiting the expression of Bax.

L31 ANSWER 2 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 1
AN 1998:711796 CAPLUS
TI Three distinct domains of SSI-1/SOCS-1/JAB protein are required for its suppression of interleukin 6 signaling
AU Narazaki, Masashi; Fujimoto, Minoru; Matsumoto, Tomoshige; Morita, Yoshiaki; **Saito, Hiroshi**; Kajita, Tadahiro; Yoshizaki, Kazuyuki; Naka, Tetsuji; **Kishimoto, Tadamitsu**
CS Department of Medicine III, Osaka University Medical School, Suita, 565-0871, Japan
SO Proc. Natl. Acad. Sci. U. S. A. (1998), 95(22), 13130-13134
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal

LA English
AB Cytokine-inducible protein SSI-1 [signal transducers and activators of transcription (STAT)-induced STAT inhibitor 1, also referred to as SOCS-1 (suppressor of cytokine signaling 1) or JAB (Janus kinase-binding protein)] neg. regulates cytokine receptor signaling by inhibition of JAK kinases. The SSI family of proteins includes eight members that are structurally characterized by an SH2 domain and a C-terminal conserved region that we have called the SC-motif. In this study, we investigated the roles of these domains in the function of SSI-1. Results of reporter assays demonstrated that the pre-SH2 domain (24 aa in front of the SH2 domain) and the SH2 domain of SSI-1 were required for the suppression by SSI-1 of interleukin 6 signaling. Coexpression studies of COS7 cells revealed that these domains also were required for inhibition of three JAKs (JAK1, JAK2, and TYK2). Furthermore, deletion of the SH2 domain, but not the pre-SH2 domain, resulted in loss of assocn. of SSI-1 with TYK2. Thus, SSI-1 assocs. with JAK family kinase via its SH2 domain, and the pre-SH2 domain is required for the function of SSI-1. Deletion of the SC-motif markedly reduced expression of SSI-1 protein in M1 cells, and this redn. was reversed by treatment with proteasome inhibitors, suggesting that this motif is required to protect the SSI-1 mol. from proteolytic degrdn. Based on these findings, we concluded that three distinct domains of SSI-1 (the pre-SH2 domain, the SH2 domain, and the SC-motif) cooperate in the suppression of interleukin 6 signaling.

L31 ANSWER 3 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 2
AN 1998:575373 CAPLUS
DN 129:288994
TI IL-6 functions in cynomolgus monkeys blocked by a humanized antibody to human IL-6 receptor
AU Imazeki, Ikuo; **Saito, Hiroyuki**; Hasegawa, Masakazu; Shinkura, Hirofumi; **Kishimoto, Tadamitsu**; Ohsugi, Yoshiyuki
CS Fuji-Gotemba Research Laboratories, Chugai Pharmaceutical Co., Ltd, Osaka, Japan
SO Int. J. Immunopharmacol. (1998), 20(7), 345-357
CODEN: IJIMDS; ISSN: 0192-0561
PB Elsevier Science Ltd.
DT Journal
LA English
AB A humanized antibody to the human interleukin-6 receptor (IL-6R), hPM-1, blocked the interleukin-6 (IL-6) functions in normal cynomolgus monkey lymphocytes in vitro. The binding activity of hPM-1 to non-human primate IL-6R was examd. in peripheral blood lymphocytes by flow cytometry. PM-1 recognized the IL-6R on T lymphocytes of cynomolgus and rhesus monkeys, but did not on those of marmosets. The homol. between human IL-6R and its cynomolgus monkey counterpart was 97.3% in the extracellular domain of the

amino acid sequence, as detd. by DNA sequencing of the PCR product from peripheral blood mononuclear cells. PM-1 inhibited two functional parameters in vitro in cynomolgus monkeys: (1), T-cell proliferation stimulated by phytohemagglutinin and human IL-6; (2), IgG-prodn. evoked by Staphylococcus aureus Cowan-1- and human IL-6-stimulated B lymphocytes. These data show that hPM-1 binds to and functionally blocks the cynomolgus monkey IL-6 receptors.

L31 ANSWER 4 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 3
AN 1997:94468 CAPLUS
DN 126:176744
TI Immunological studies of SK2 hybridoma cells microencapsulated with alginate-poly(L)-lysine-alginate (AP) membrane following allogeneic transplantation
AU Okada, Naoki; Miyamoto, Hajime; Yoshioka, Tatsunobu; Sakamoto, Kayoko; **Katsume, Asao**; **Saito, Hiroyuki**; Nakagawa, Shinsaku; Ohsugi, Yoshiyuki; Mayumi, Tadanori
CS Fac. and Grad. Sch. Pharmaceutical Sci., Osaka Univ., Oaka, 565, Japan
SO Biochem. Biophys. Res. Commun. (1997), 230(3), 524-527
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
AB Microencapsulation of living cells or tissues has been proposed to prevent their immune destruction following transplantation. In this study, we examd. whether SK2 hybridoma cells microencapsulated in an alginate-poly(L)lysine-alginate (APA) membrane (APA-SK2 cells) were immunoisolated from the allogeneic host's immune system using a cytotoxicity test. The APA membrane inhibited the activation of the host's cellular immune response, but did not prevent the prodn. of cytotoxic antibodies against entrapped SK2 cells following allogeneic transplantation. However, the APA-SK2 cells remained vital in SK2 cell-immunized mice as well as in intact mice. We considered that complement regulatory factors which were present on cell membrane and had species-specific restriction blocked the complement-mediated cell lysis on allogeneic transplantation, since APA-SK2 cells were destroyed by rabbit anti-SK2 cells antiserum. Our results demonstrated that APA membrane could inhibit cell-cell contact between entrapped cells and the host's lymphocytes, but could not completely protect the entrapped cells from xenogeneic humoral immunity.

L31 ANSWER 5 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 4
AN 1997:206219 CAPLUS
DN 126:297556
TI Therapeutic effect of cytomedicine on mesangio-proliferative glomerulonephritis in human interleukin-6 transgenic mice
AU Okada, Naoki; Miyamoto, Hajime; Yoshioka, Tatsunobu; **Katsume,**

Asao; Saito, Hiroyuki; Yorozu, Keigo; Ueda, Otoya;
Nakagawa, Shinsaku; Ohsugi, Yoshiyuki; Mayumi, Tadanori
CS Faculty and Graduate School of Pharmaceutical Sciences, Osaka University, Suita, 565, Japan
SO Biol. Pharm. Bull. (1997), 20(3), 255-258
CODEN: BPBLEO; ISSN: 0918-6158
PB Pharmaceutical Society of Japan
DT Journal
LA English
AB We previously demonstrated that IgG1 plasmacytosis in human interleukin-6 transgenic mice (hIL-6 Tgm) was suppressed by the implantation of SK2 hybridoma cells (SK2 cells, which secrete anti-hIL-6 monoclonal antibodies) microencapsulated in a semipermeable and biocompatible device. In this study, we demonstrated that the mesangio-proliferative glomerulonephritis in hIL-6 Tgm was also improved by the same treatment. These results strongly support the concept of cytomedicine, which is a novel drug delivery system (DDS) using living cells. However, an electron microscopy study showed that cytomedicine has a limited duration of effectiveness because of the disappearance of space for cell proliferation in the microcapsule. Thus, the control of cell proliferation in a device must be developed to prolong the function and effectiveness of cytomedicine.

L31 ANSWER 6 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 5
AN 1996:693193 CAPLUS
DN 126:135486
TI Medical application of microencapsulating hybridoma cells in agarose microbeads 'cytomedicine': therapeutic effect on IgG1 plasmacytosis and mesangio-proliferative glomerulonephritis in the interleukin 6 transgenic mouse
AU Okada, Naoki; Miyamoto, Hajime; Kaneda, Yoshihisa; Yamamoto, Yoko; **Katsume, Asao**; **Saito, Hiroyuki**; Yorozu, Keigo; Ueda, Otoya; Tsutsumi, Yasuo; et al.
CS Faculty and Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka, Japan
SO J. Controlled Release (1997), 44(2,3), 195-200
CODEN: JCREEC; ISSN: 0168-3659
PB Elsevier
DT Journal
LA English
AB We conducted preliminary studies to examine the feasibility of using microencapsulated living cells as carriers of bioactive drugs ('cytomedicine') to test our premise that such a novel drug delivery system would have certain advantages as a long-term delivery system for hormones, enzymes and other biomols. in vivo. As graft rejection occurs when living cells are implanted in allogeneic or xenogeneic recipients, accordingly we used agarose microencapsulation technique to prevent destruction of the implanted

cells by the host's immune system. Human interleukin 6 (hIL-6) transgenic mice, which develop massive IgG1 plasmacytosis and mesangio-proliferative glomerulonephritis with age, were i.p. injected with agarose microbeads contg. SK2 hybridoma cells (SK2 cells), which secrete anti-hIL-6 monoclonal antibodies. These mice demonstrated therapeutic response with reduced IgG1 plasmacytosis and proteinuria, and they also showed prolongation of survival time compared with the untreated group. These results are encouraging evidence that cytomedicine has potential application as an effective long-term delivery system of bioactive drugs in vivo.

L31 ANSWER 7 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 6
AN 1997:114999 CAPLUS
DN 126:170310
TI Interleukin-6 overexpression cannot generate serious disorders in severe combined immunodeficiency mice
AU **Katsume, Asao**; Miyai, Tatsuya; Suzuki, Hiroshi; Moriguchi, Yoshiyuki; Kawata, Hiromitsu; Tatsumi, Tetsuo; Suematsu, Sachiko; **Kishimoto, Tadamitsu**; Ohsugi, Yoshiyuki
CS Fuji-Gotemba Research Laboratories, Chugai Pharmaceutical Co. Ltd., Shizuoka, 412, Japan
SO Clin. Immunol. Immunopathol. (1997), 82(2), 117-124
CODEN: CLIIAT; ISSN: 0090-1229
PB Academic
DT Journal
LA English
AB C57BL/6 human interleukin-6 (IL-6) transgenic mice develop mesangial proliferative glomerulonephritis with massive IgG1 plasmacytosis and die of renal failure in early life. To test whether the IL-6 overexpression could cause development of mesangial proliferative glomerulonephritis without plasmacytosis or promote proliferation of immature B cells that have not undergone Ig gene rearrangement, the IL-6 transgene was introduced into mice with severe combined immunodeficiency (SCID). In the immunocompetent littermate IL-6 transgenic mice, there were various symptoms such as plasmacytosis, nephropathy, anemia, and thrombocytosis, accompanied by marked increases in serum IL-6 levels as they aged. All these mice died by 25 wk of age. In contrast, the SCID-IL-6 transgenic mice had no such abnormalities, except certain hematol. changes, although the transgene was expressed in various tissues. In these mice, the serum IL-6 levels were 10-15-fold higher than those in the nontransgenic mice, and they remained const. throughout their lives. Furthermore, there were no signs of lymphoid development. Thus, deregulation of IL-6 expression does not stimulate cell growth or differentiation of immature B cells, and does not result in plasmacytosis and age-related increases in IL-6 prodn., and also does not generate mesangial proliferative glomerulonephritis.

L31 ANSWER 8 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 7

AN 1997:458131 CAPLUS
DN 127:140328
TI Development of novel drug delivery system of bioactive molecules from "cytomedicine" using hybridoma cells entrapped in alginate-poly(L-lysine)-alginate microcapsules
AU Yoshioka, Tatsunobu; Okada, Naoki; Miyamoto, Hajime; Sakamoto, Kayoko; **Katsume, Asao**; **Saito, Hiroyuki**; Yorozu, Keigo; Ueda, Otoya; Nakagawa, Shinsaku; Ohsugi, Yoshiyuki; Mayumi, Tadanori
CS Fac. and Grad. Sch. Pharm. Sci., Osaka Univ., Suita, 565, Japan
SO Drug Delivery Syst. (1997), 12(2), 107-114
CODEN: DDSYEI; ISSN: 0913-5006
PB Nippon DDS Gakkai Jimukyoku
DT Journal
LA Japanese
AB A novel drug delivery systems (DDS) "cytomedicine" was developed using living cells entrapped in alginate-poly(L-lysine)-alginate (APA) microcapsules which has a selective semipermeable characteristic. Because the APA membrane allows small mols. such as glucose and nutrients to diffuse freely but prevents the passage of large mols. and cells, entrapped cells are isolated from the host's immune system. In this study, we examd. the effects of mol. wt. of poly(L-lysine) on the properties of APA-microencapsulated SK2 hybridoma cells (APA-SK2 cells), which secrete the anti-human interleukin 6 (hIL-6 Tgm). Single i.p. injection of APA-SK2 cells improved IgG1 plasmacytosis and mesangio-proliferative glomerulonephritis in hIL-6 Tgm. This indicated that the cytomedicine is very effective for long-term delivery of bioactive mols. in vivo.

L31 ANSWER 9 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 8
AN 1997:544874 CAPLUS
DN 127:243843
TI Cloning and functional analysis of new members of STAT induced STAT inhibitor (SSI) family: SSI-2 and SSI-3
AU Minamoto, Seijiro; Ikegame, Kazuhiro; Ueno, Kiyonobu; Narazaki, Masashi; Naka, Tetsuji; Yamamoto, Hiroyasu; Matsumoto, Tomoshige; **Saito, Hiroshi**; Hosoe, Shigeto; **Kishimoto, Tadamitsu**
CS Department of Medicine III, Osaka University Medical School, Suita, 565, Japan
SO Biochem. Biophys. Res. Commun. (1997), 237(1), 79-83
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
AB Upon the corresponding ligand's stimulation, the cytokine receptors activate several signal pathways: JAK-STAT pathway, Ras-MAP kinase pathway and so on. Recently, we demonstrated that one of the STAT3 (signal transducer and activator of transcription-3) target genes

could suppress the function of STAT3 and designated it SSI-1 (STAT-induced STAT inhibitor-1). SSI-1 is thought to play a crit. role in neg. feedback control of JAK-STAT signaling pathway. In the present study, we identified two novel human genes which products have homologous region in their SH2 domain and its COOH-terminal region to mouse SSI-1. Northern blotting anal. and functional studies demonstrated that SSI-2 and SSI-3 mRNA were also induced by cytokine stimulation and their forced expression in mouse myeloid leukemia cell, M1, suppressed the apoptotic effect of LIF, like SSI-1. We also demonstrated the structure of human SSI-1.

L31 ANSWER 10 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 9
AN 1997:75834 CAPLUS
DN 126:203608
TI Cytomedical therapy for IgG1 plasmacytosis in human interleukin-6 transgenic mice using hybridoma cells microencapsulated in alginate-poly(L-lysine)-alginate membrane
AU Okada, Naoki; Miyamoto, Hajime; Yoshioka, Tatsunobu; **Katsume, Asao; Saito, Hiroyuki**; Yorozu, Keigo; Ueda, Otoya; Itoh, Norio; Mizuguchi, Hiroyuki; Nakagawa, Shinsaku; Ohsugi, Yoshiyuki; Mayumi, Tadanori
CS Faculty and Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka, 565, Japan
SO Biochim. Biophys. Acta (1997), 1360(1), 53-63
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier
DT Journal
LA English
AB Cytomedical therapy for human interleukin-6 transgenic mice (hIL-6 Tgm) was implemented by the i.p. injection of alginate-poly(L)lysine-alginate (APA) membranes microencapsulating SK2 hybridoma cells (APA-SK2 cells) which secrete anti-hIL-6 monoclonal antibodies (SK2 mAb). IgG1 plasmacytosis in the hIL-6 Tgm was suppressed by a single injection of APA-SK2 cells, and the survival time of these mice was remarkably prolonged. The viable cell no. and the SK2 mAb-secretion of APA-SK2 cells increased for at least one month both under culture conditions and in allogeneic recipients (in vivo). Moreover, SK2 mAb which were secreted from APA-SK2 cells injected into allogeneic recipients was detected in serum at high concns.; 3-5 mg/mL from day 14 to day 50 post-injection. In contrast, the injection of free SK2 cells had no therapeutic effect on hIL-6 Tgm. These results strongly suggest that APA membranes microencapsulating cells which were modified to secrete mols. useful for the treatment of a disorder were effective as an in vivo long-term delivery system of bioactive mols., as 'cytomedicine'.

L31 ANSWER 11 OF 23 JICST-EPlus COPYRIGHT 1999 JST
AN 980776484 JICST-EPlus
TI Examination on immunogenicity and immunity isolation of cellular

drugs.
AU OKADA NAOKI; MIYAMOTO HAJIME; YOSHIOKA TATSUNOBU; SAKAMOTO KAYOKO; NAKAGAWA SHINSAKU; MAYUMI TADANORI
KATSUME ASAO; **SAITO HIROYUKI**; OSUGI YOSHIMASA
CS Osaka Univ., Fac. of Pharm. Sci.
Chugai Pharm. Co., Ltd.
SO Nippon Yakugakkai Nenkai Koen Yoshishu, (1997) vol. 117th, no. 4, pp. 34. Journal Code: L0914A
ISSN: 0918-9823
CY Japan
LA Japanese
STA New

L31 ANSWER 12 OF 23 JICST-EPlus COPYRIGHT 1999 JST
AN 980776483 JICST-EPlus
TI Extension of effective therapy period by multiple administration of cellular drug.
AU MIYAMOTO HAJIME; OKADA NAOKI; YOSHIOKA TATSUNOBU; SAKAMOTO KAYOKO; NAKAGAWA SHINSAKU; MAYUMI TADANORI
KATSUME ASAO; **SAITO HIROYUKI**; OSUGI YOSHIMASA
CS Osaka Univ., Fac. of Pharm. Sci.
Chugai Pharm. Co., Ltd.
SO Nippon Yakugakkai Nenkai Koen Yoshishu, (1997) vol. 117th, no. 4, pp. 34. Journal Code: L0914A
ISSN: 0918-9823
CY Japan
LA Japanese
STA New

L31 ANSWER 13 OF 23 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 96-230370 [23] WPIDS
DNC C96-072766
TI Agent for prevention and treatment of diseases caused by interleukin-6 prodn. - contains antibody recognising interleukin-6 receptor, useful against plasma-cytosis, anaemia, nephritis etc.
DC B04 D16
IN KATSUME, T; **KISHIMOTO, T**; **SAITO, H**;
KATSUME, A
PA (KISH-I) KISHIMOTO T; (CHUS) CHUGAI PHARM CO LTD; (KISH-I) KISHIMOTO C; (CHUS) CHUGAI SEIYAKU KK
CYC 66
PI WO 9612503 A1 960502 (9623)* JA 49 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS KE KG KR KZ LK LR LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN
AU 9537099 A 960515 (9634)
JP 08169846 A 960702 (9636) 14 pp
Searcher : Shears 308-4994

NO 9701816 A 970618 (9735)
FI 9701669 A 970617 (9738)
EP 791359 A1 970827 (9739) EN 31 pp
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
CZ 9701189 A3 970917 (9743)
HU 77035 T 980302 (9821)
AU 689657 B 980402 (9823)
KR 97706846 A 971201 (9847)
ADT WO 9612503 A1 WO 95-JP2169 951020; AU 9537099 A AU 95-37099 951020; JP 08169846 A JP 95-272893 951020; NO 9701816 A WO 95-JP2169 951020, NO 97-1816 970418; FI 9701669 A WO 95-JP2169 951020, FI 97-1669 970418; EP 791359 A1 EP 95-934866 951020, WO 95-JP2169 951020; CZ 9701189 A3 WO 95-JP2169 951020, CZ 97-1189 951020; HU 77035 T WO 95-JP2169 951020, HU 97-1900 951020; AU 689657 B AU 95-37099 951020; KR 97706846 A WO 95-JP2169 951020, KR 97-702588 970419
FDT AU 9537099 A Based on WO 9612503; EP 791359 A1 Based on WO 9612503; CZ 9701189 A3 Based on WO 9612503; HU 77035 T Based on WO 9612503; AU 689657 B Previous Publ. AU 9537099, Based on WO 9612503; KR 97706846 A Based on WO 9612503
PRAI JP 94-257010 941021
AN 96-230370 [23] WPIDS
AB WO 9612503 A UPAB: 960610
An agent for the prevention and treatment of diseases caused by interleukin-6 prodn. contains an antibody recognising the interleukin-6 receptor (IL-6R).

USE - The antibody is used in the treatment and prevention of diseases in which interleukin-6 is implicated, such as plasmacytosis (causing rheumatism or Castleman's disease), high immunoglobulin levels in blood, anaemia and nephritis (including nephritis involving mesangium hyperplasia).
Dwg.12/18

L31 ANSWER 14 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 10
AN 1997:2616 CAPLUS
DN 126:73597
TI Anti-interleukin-6 receptor antibody prevents muscle atrophy in colon-26 adenocarcinoma-bearing mice with modulation of lysosomal and ATP-ubiquitin-dependent proteolytic pathways
AU Fujita, Junya; Tsujinaka, Toshimasa; Yano, Masahiko; Ebisui, Chikara; **Saito, Hiroyuki**; **Katsume, Asao**; Akamatsu, Ken-ichi; Ohsugi, Yoshiyuki; Shiozaki, Hitoshi; Monden, Morito
CS Department Surgery II, Osaka University Medical School, Suita, 565, Japan
SO Int. J. Cancer (1996), 68(5), 637-643
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss
DT Journal
LA English

AB Progression of skeletal muscle atrophy is one of the characteristic features in cancer patients. Interleukin-6 (IL-6) has been reported to be responsible for the loss of lean body mass during cancer cachexia in colon-26 adenocarcinoma (C-26)-bearing mice. This study was carried out to elucidate the intracellular proteolytic pathways operating in skeletal muscle in C-26-bearing mice, and to examine the effect of anti IL-6 receptor antibody on muscle atrophy. On day 17 after tumor inoculation, the gastrocnemius muscle wt. of C-26-bearing mice had decreased to 69% of that of the pair-fed control mice. This wt. loss occurred in assocn. with increases in the mRNA levels of cathepsins B and L, poly-ubiquitin (Ub), and the subunits of proteasomes in the muscles. Furthermore, enzymic activity of cathepsin B+L in the muscles also increased to 119% of the control. The administration of antimurine IL-6 receptor antibody to C-26-bearing mice reduced the wt. loss of the gastrocnemius muscles to 84% of that of the control mice, whose enzymic activity of cathepsin B+L and mRNA levels of cathepsin L and poly-Ub were suppressed compared with those of the C-26-bearing mice. Thus, both the lysosomal cathepsin pathway and the ATP-dependent proteolytic pathway might be involved in the muscle atrophy of C-26-bearing mice. The results also suggest that anti IL-6 receptor antibody could be a potential therapeutic agent against muscle atrophy in cancer cachexia by inhibiting these proteolytic systems.

L31 ANSWER 15 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 11
AN 1995:281634 CAPLUS
DN 122:72318
TI Murine fibroblast growth factor receptor 1 gene generates multiple messenger RNAs containing two open reading frames via alternative splicing
AU Harada, Tasuku; **Saito, Hiroshi**; Kouhara, Haruhiko; Kurebayashi, Shogo; Kasayama, Soji; Terakawa, Naoki; **Kishimoto, Tadamitsu**; Sato, Bunzo
CS Dep. of Obstetrics and Gynecology, Tottori Univ., Tottori, 683, Japan
SO Biochem. Biophys. Res. Commun. (1994), 205(2), 1057-63
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB The arrangement of exons and introns encoding 5'-side of murine fibroblast growth factor (FGF) receptor 1 (FGFR-1) gene was mapped. A large intron with a size of 14 kb was identified between exon 1 and exon 2. In addn., all FGFR-1 subtypes including a unique variant form with 12 amino acids insertion and two amino acids deletion were obsd. to be able to be generated through alternative splicing. Furthermore, complete sequencing of the 5'-region of FGFR-1 mRNA revealed that a relatively large open reading frame precedes the major open reading frame encoding FGFR-1. These

results indicate that FGFR-1 mRNAs are uniquely translated from an internal translation start site.

L31 ANSWER 16 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 12
AN 1994:237353 CAPLUS
DN 120:237353
TI Mapping of a transcription element critical for expression of the fibroblast growth factor receptor 1 gene
AU **Saito, Hiroshi**; Kouhara, Haruhiko; Harada, Tasuku; Miyake, Seigou; Sugiyama, Haruo; **Kishimoto, Tadamitsu**; Sato, Bunzo
CS Med. Sch., Osaka Univ., Suitashi, 565, Japan
SO Biochem. Biophys. Res. Commun. (1994), 198(3), 1020-6
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB The fibroblast growth factor receptor 1 (FGFR1) gene has no TATA or CCAAT-elements. To examine its mechanism of expression, the authors characterized the transcription element of this gene. The basal promoter element was mapped to the 5'-flanking region from -89 to -43. The DNAse I protection assay and gel shift anal. revealed that a nuclear protein extd. from FGFR1-expressing cells (NIH3T3 and SC-3), but not from FGFR1-nonexpressing cells (P3U1), could bind to the nucleotide sequence from -62 to -42. The mol. wt. of this protein was .apprx.100 kDa by Southwestern anal. In addn., both the promoter activity and the nuclear protein binding activity were markedly impaired by the substitution of two bases within this footprint site. Interestingly, this footprint site appeared to lack the consensus sequence of the currently reported transcription factors. These results indicate that the 5'-flanking region from -62 to -42 plays a pivotal role in FGFR1 gene expression.

L31 ANSWER 17 OF 23 JICST-EPlus COPYRIGHT 1999 JST
AN 950180388 JICST-EPlus
TI Suppression by anti-IL-6 receptor antibody of disorders due to an IL-6 overexpression in IL-6 transgenic mice.
AU **KATSUME ASAO**; **SAITO HIROYUKI**; KOISHIHARA YASUO; AKAMATSU KEN'ICHI; MIYAI TATSUYA; OSUGI YOSHIYUKI **KISHIMOTO TADAMITSU**
CS Chugai Pharm. Co., Ltd.
Osaka Univ., Med. Sch.
SO Nippon Men'eki Gakkai Sokai, Gakujutsu Shukai Kiroku, (1994) vol. 24, pp. 496. Journal Code: Z0383B
CY Japan
LA Japanese
STA New

L31 ANSWER 18 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 13
AN 1994:103478 CAPLUS
DN 120:103478

TI Androgen-induced growth factor and its receptor: demonstration of the androgen-induced autocrine loop in mouse mammary carcinoma cells
AU Sato, Bunzo; Kouhara, Haruhiko; Koga, Masafumi; Kasayama, Soji; **Saito, Hiroshi**; Sumitani, Satoru; Hashimoto, Kunihiko; **Kishimoto, Tadamitsu**; Tanaka, Akira; Matsumoto, Keishi
CS Sch. Med., Osaka Univ., Suita, 565, Japan
SO J. Steroid Biochem. Mol. Biol. (1993), 47(1-6), 91-8
CODEN: JSBBEZ; ISSN: 0960-0760
DT Journal; General Review
LA English
AB A review, with 40 refs., of the involvement of growth factors in androgen-induced growth of transformed cells using SC-3 cells derived from mouse mammary carcinoma (Shionogi carcinoma 115). Topics discussed were: secretion of growth factor in response to androgen-induced stimulation of SC-3 cells; crit. role of AIGF in androgen-induced growth of SC-3 cells; condensation on or near SC-3 cells of secreted AIGF and its activation by glycosaminoglycans; FGF receptor 1 variant form as AIGF receptor; and upregulation of FGF receptor 1 mRNA by androgens and AIGF.

L31 ANSWER 19 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 14
AN 1992:188935 CAPLUS
DN 116:188935
TI Characterization of the promoter region of the murine fibroblast growth factor receptor 1 gene
AU **Saito, Hiroshi**; Kouhara, Haruhiko; Kasayama, Soji; **Kishimoto, Tadamitsu**; Sato, Bunzo
CS Dep. Intern. Med. III, Osaka Univ. Hosp., Osaka, 553, Japan
SO Biochem. Biophys. Res. Commun. (1992), 183(2), 688-93
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB The promoter region of the fibroblast growth factor (FGF) receptor 1 (FGFR 1) was cloned from genomic library of mouse FGF-responsive cell lines. The genomic clone isolated here includes the FGFR 1 gene from position -868 to +697 relative to the transcription initiation site. Sequence anal. reveals the presence of various consensus sequences for the binding sites of transcriptional factors such as SP 1, GCF, Oct-I, AP 1 and AP 2, but the absence of TATA and CAAT sequence motif. The transfection of this promoter-CAT constructs into NIH 3T3 cells demonstrates its promoter activity which is located between base -106 and +104.

L31 ANSWER 20 OF 23 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 15
AN 1991:551752 CAPLUS
DN 115:151752
TI Stimulation of biosynthesis of nerve growth factor by acidic fibroblast growth factor in cultured mouse astrocytes
AU Ono, Takashi; **Saito, Hiroko; Kishimoto, Toshimitsu**

; Okumoto, Takeki; Miyamoto, Kanji
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Iruma, 358, Japan
SO Neurosci. Lett. (1991), 126(1), 18-20
CODEN: NELED5; ISSN: 0304-3940
DT Journal
LA English
AB Bovine acidic and basic fibroblast growth factors (aFGF and bFGF) dose-dependently stimulated the release of nerve growth factor (NGF) in a culture medium of mouse astrocytes. On addn. of a FGF, NGF concn. in the medium started to increase compared to that of the control cultures after 4 h and was further sustained for 24 h. The content of NGF mRNA in the astrocytes treated with aFGF peaked at 8-fold over the control level after 4 h. The astrocytes did not proliferate until after 72 h when treated with FGFs under the conditions employed. Evidently, a FGF stimulates the biosynthesis of NGF in cultured astrocytes without promoting cell proliferation.

L31 ANSWER 21 OF 23 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 16
AN 1991:49554 BIOSIS
DN BA91:27835
TI SIGNIFICANT INCREASE OF INTERLEUKIN 6 PRODUCTION IN BLOOD MONONUCLEAR LEUKOCYTES OBTAINED FROM PATIENTS WITH ACTIVE INFLAMMATORY BOWEL DISEASE.
AU SUZUKI Y; **SAITO H**; KASANUKI J; **KISHIMOTO T**; TAMURA Y; YOSHIDA S
CS 2ND DEP. INTERN. MED., CHIBA UNIV., SCH. MED., CHIBA 280, JPN.
SO LIFE SCI, (1990) 47 (24), 2193-2198.
CODEN: LIFSAK. ISSN: 0024-3205.
FS BA; OLD
LA English
AB In the present study, we compared the potency of interleukin 6 production in peripheral blood mononuclear leukocytes between paired patients with active stage and inactive stage of inflammatory bowel disease. Subjects included nine patients with ulcerative colitis, ten patients with Crohn's disease and sex-matched nine healthy volunteers. Mononuclear leukocytes were stimulated with concanavalin A for 24 h to induce interleukin 6 production. Interleukin 6 content in the culture medium was assayed by using specific ELISA and interleukin 6 dependent cell line MH-60. Interleukin 6 production was found to be significantly increased in mononuclear leukocytes from both active ulcerative colitis and Crohn's disease as compared to that from control subjects. There was no significant difference in interleukin 6 production between ulcerative colitis and Crohn's disease. The potency of interleukin 6 production was returned to the control level when the diseases became inactive. The present results, therefore, may indicate some important role of interleukin 6 in the pathogenesis of inflammatory bowel disease and also the potency of interleukin 6 production in mononuclear leukocytes can be an indicator of the activity of inflammatory bowel disease.

Searcher : Shears 308-4994

L31 ANSWER 22 OF 23 JICST-EPlus COPYRIGHT 1999 JST
AN 900539646 JICST-EPlus
TI Clinical study of KRN8601 (rhG-CSF) on leukopenia induced by chemotherapy for urogenital cancer.
AU ASO YOSHIO; AKAZA HIDEYUKI; TAKAHISA FUMIMARO
TAZAKI HIROSHI
KISHIMOTO TAKASHI
KOISO KENKICHI
SAITO HIROSHI
KOTAKE TOSHIHIKO
SONODA TAKAO
CS Univ. of Tokyo, Faculty of Medicine
Keio Univ., School of Medicine
Nihon Univ., School of Medicine
Univ. of Tsukuba, Inst. of Clinical Medicine
Saitama Medical School, General Medical Center
Center for Adult Diseases, Osaka
Osaka Univ., Medical School
SO Hinyoki Geka (Japanese Journal of Urological Surgery), (1990) vol. 3, no. 5, pp. 677-686. Journal Code: L0465A (Fig. 3, Tbl. 13, Ref. 8)
ISSN: 0914-6180
CY Japan
DT Journal; Article
LA Japanese
STA New

L31 ANSWER 23 OF 23 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 17
AN 1983:176445 BIOSIS
DN BA75:26445
TI INDUCTION OF THE DIFFERENTIATION OF MEMORY T KILLER CELLS WITH FACTORS RELEASED FROM MACROPHAGE-LIKE CELL LINES.
AU IGARASHI T; IKEDA Y; **SAITO H**; TAKANO S; **KISHIMOTO T**; SHIDA T
CS IIIRD DEP. INTERN. MED., OSAKA UNIV. MED. SCH., FUKUSHIMA, OSAKA 553, JPN.
SO CELL IMMUNOL, (1982) 70 (1), 11-26.
CODEN: CLIMB8. ISSN: 0008-8749.
FS BA; OLD
LA English
AB Mouse macrophage-like cell lines J774.1 and WEHI-3 as well as peritoneal exudate macrophages have been demonstrated to produce factors which induce the differentiation of memory cells into specific T killer cells in the absence of an added antigen. Lipopolysaccharide stimulation was required for J774.1 cells and peritoneal macrophages to produce the factors but not for WEHI-3 cells. Interferon seemed to be one of the responsible factors. Macrophages seem to produce other active factors; 1 has a MW of >